

Package leaflet: Information for the user

ZYDOL[®] 50 mg/ml Solution for Injection

Tramadol hydrochloride

This medicine contains tramadol which is an opioid, which can cause addiction. You can get withdrawal symptoms if you stop taking it suddenly.

Read all of this leaflet carefully before you start taking 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 pharmacist.
- This medicine has been provided for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet (section 4).

In this leaflet:

1. What ZYDOL[®] Solution for Injection is and what it is used for
2. What you need to know before you receive ZYDOL[®] Solution for Injection
3. How to take ZYDOL[®] Solution for Injection
4. Possible side effects
5. How to store ZYDOL[®] Solution for Injection
6. Contents of the pack and other information

1. What ZYDOL Solution for Injection is and what it is used for

ZYDOL Solution for Injection has been given to you for the treatment of moderate to severe pain.

Tramadol - the active substance in ZYDOL Solution for Injection belongs to a class of medicines called opioids, which are 'pain relievers'.

This medicine has been given to you and should not be given to anyone else. Opioids can cause addiction and you may get withdrawal symptoms if you stop taking it suddenly. Your prescriber should have explained how long you will be taking it for and when it is appropriate to stop, how to do this safely.

2. What you need to know before you receive ZYDOL Solution for Injection

Do not take ZYDOL Solution for Injection

- if you are allergic to tramadol or any of the other ingredients of this medicine (listed in section 6);
- in acute poisoning with alcohol, sleeping pills, pain relievers or other psychotropic medicines (medicines that affect mood and emotions);
- if you are also taking MAO inhibitors (certain medicines used for treatment of depression) or have taken them in the last 14 days before treatment with ZYDOL Solution for Injection (see "Other medicines and ZYDOL Solution for Injection");
- if you are an epileptic and your fits are not adequately controlled by treatment;
- as a substitute in drug withdrawal.

Warnings and precautions

Talk to your doctor before receiving ZYDOL Solution for Injection if you:

- are or have ever been addicted to opioids, alcohol, prescription medicines, or illegal drugs;
- have previously suffered from withdrawal symptoms such as agitation, anxiety, shaking or sweating when you have stopped taking alcohol or drugs;
- feel you need to take more of ZYDOL Solution for Injection to get the same level of pain relief, this may mean you are becoming tolerant to the effects of this medicine or are becoming addicted to it. Speak to your prescriber who will discuss your treatment and may change your dose or switch you to an alternative pain reliever;
- suffer from consciousness disorders (if you feel that you are going to faint);
- are in a state of shock (cold sweat may be a sign of this);
- suffer from increased pressure in the brain (possibly after a head injury or brain disease);
- have difficulty in breathing;
- have a tendency towards epilepsy or fits because the risk of a fit may increase;
- suffer from depression and you are taking antidepressants as some of them may interact with tramadol (see “Other medicines and ZYDOL Solution for Injection”);
- suffer from a liver or kidney disease.

Sleep-related breathing disorders

ZYDOL Solution for Injection contains an active substance that belongs to the group of opioids. Opioids can cause sleep-related breathing disorders, for example central sleep apnea (shallow/pause of breathing during sleep) and sleep-related hypoxemia (low level of oxygen in the blood).

The risk of experiencing central sleep apnea is dependent on the dose of opioids. Your doctor may consider decreasing your total opioid dosage if you experience central sleep apnea.

There is a small risk that you may experience a so-called serotonin syndrome that can occur after having taken tramadol in combination with certain antidepressants or tramadol alone. Seek medical advice immediately if you have any of the symptoms related to this serious syndrome (see section 4 “Possible side effects”).

Epileptic fits have been reported in patients taking tramadol at the recommended dose level. The risk may be increased when doses of tramadol exceed the recommended upper daily dose limit (400 mg).

Taking this medicine regularly, particularly for a long time, can lead to addiction. Your prescriber should have explained how long you will be taking it for and when it is appropriate to stop, how to do this safely.

Rarely, increasing the dose of this medicine can make you more sensitive to pain. If this happens, you need to speak to your prescriber about your treatment.

Addiction can cause withdrawal symptoms when you stop taking this medicine. Withdrawal symptoms can include restlessness, difficulty sleeping, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increased blood pressure, feeling or being sick, diarrhoea, loss of appetite, shaking, shivering or sweating. Your prescriber will discuss with you how to gradually reduce your dose before stopping the medicine. It is important that you do not stop taking the medicine suddenly as you will be more likely to experience withdrawal symptoms.

Opioids should only be used by those they are prescribed for. Do not give your medicine to anyone else. Taking higher doses or more frequent doses of opioid, may increase the risk of addiction. Overuse and misuse can lead to overdose and/or death.

Tramadol is transformed in the liver by an enzyme. Some people have a variation of this enzyme and this can affect people in different ways. In some people, they may not get enough pain relief but other people are more likely to get serious side effects. If you notice any of the following side effects, you must stop taking this medicine and seek immediate medical advice: slow or shallow breathing, confusion, sleepiness, small pupils, feeling or being sick, constipation, lack of appetite.

Talk to your doctor if you experience any of the following symptoms while taking ZYDOL Solution for Injection:

Extreme fatigue, lack of appetite, severe abdominal pain, nausea, vomiting or low blood pressure. This may indicate that you have adrenal insufficiency (low cortisol levels). If you have these symptoms, contact your doctor, who will decide if you need to take hormone supplement.

Other medicines and ZYDOL Solution for Injection

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

ZYDOL Solution for Injection should not be taken together with MAO inhibitors (certain medicines for the treatment of depression).

The pain-relieving effect of ZYDOL Solution for Injection may be reduced and the length of time it acts may be shortened, if you take medicines which contain

- carbamazepine (for epileptic fits);
- ondansetron (prevents nausea).

Your doctor will tell you whether you should take ZYDOL Solution for Injection, and what dose.

The risk of side effects increases,

- if you are taking other pain relievers such as morphine and codeine (also as cough medicine), and alcohol while you are taking ZYDOL Solution for Injection. You may feel drowsier or feel that you might faint. If this happens tell your doctor.
- Concomitant use of Zydol Solution for Injection and tranquillizers or sleeping pills (e.g. benzodiazepines), increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible. However, if your doctor gives Zydol Solution for Injection together with sedating medicines the dose and the duration of concomitant treatment should be limited by your doctor. Please tell your doctor about all sedating medicines you are taking, and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.
- if you are taking medicines which may cause convulsions (fits), such as certain antidepressants or antipsychotics. The risk having a fit may increase if you take ZYDOL Solution for Injection at the same time. Your doctor will tell you whether ZYDOL Solution for Injection is suitable for you.
- if you are taking certain antidepressants ZYDOL Solution for Injection may interact with these medicines and you may experience serotonin syndrome (see section 4 "Possible side effects").
- if you are taking coumarin anticoagulants (medicines for blood thinning), e.g. warfarin, together with ZYDOL Solution for Injection. The effect of these medicines on blood clotting may be affected and bleeding may occur.

ZYDOL Solution for Injection with food and alcohol

Do not drink alcohol during treatment with ZYDOL Solution for Injection as its effects may be intensified.

Children and adolescents

Use in children with breathing problems:

Tramadol is not recommended in children with breathing problems, since the symptoms of tramadol toxicity may be worse in these children.

Pregnancy, breast-feeding and fertility

Do not take ZYDOL Solution for Injection if you are pregnant or think you might be pregnant unless you have discussed this with your prescriber and the benefits of treatment are considered to outweigh the potential harm to the baby.

If you use ZYDOL Solution for Injection during pregnancy, your baby may become dependent and experience withdrawal symptoms after the birth which may need to be treated.

Do not take ZYDOL Solution for Injection while you are breastfeeding as tramadol passes into breast milk and will affect your baby.

Based on human experience tramadol is suggested not to influence female or male fertility

Driving and using machines

ZYDOL Solution for Injection may cause drowsiness, dizziness and blurred vision and therefore may impair your reactions. If you feel that your reactions are affected, do not drive a car or other vehicle, do not use electric tools or operate machinery.

The medicine can affect your ability to drive as it may make you sleepy or dizzy.

- Do not drive while taking this medicine until you know how it affects you.
- It is an offence to drive if this medicine affects your ability to drive.
- However, you would not be committing an offence if:
 - The medicine has been given to treat a medical or dental problem and
 - You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
 - It was not affecting your ability to drive safely

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine.

Information on sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per ml, i.e. essentially 'sodium-free'.

3. How to use ZYDOL Solution for Injection

The dosage should be adjusted to the intensity of your pain and your individual pain sensitivity. In general the lowest pain-relieving dose should be received. Normally, daily doses up to 8 ml of ZYDOL solution for injection (equivalent to 400 mg tramadol hydrochloride) will be sufficient. Exceptionally, if clinically required, your doctor may direct to use a higher daily dose.

Unless otherwise prescribed by your doctor, the usual dose is:

Adults and adolescents from the age of 12 years:

Depending on your pain you will receive 1-2 ml of ZYDOL Solution for Injection (equivalent to 50 – 100 mg tramadol hydrochloride). Depending on your pain the effect lasts for about 4-8 hours.

Your doctor may prescribe a different, more appropriate dosage of ZYDOL Solution for Injection.

Children

ZYDOL Solution for Injection is not suitable for children below the age of 12 years.

Elderly patients

In elderly patients (above 75 years) the excretion of tramadol may be delayed. If this applies to you, your doctor may direct to prolong the dosage interval.

Severe liver or kidney disease (insufficiency)/dialysis patients

Patients with severe liver and/or kidney insufficiency should not receive ZYDOL Solution for Injection. If in your case the insufficiency is mild or moderate, your doctor may recommend prolonging the dosage interval.

How and when should you receive ZYDOL Solution for Injection?

ZYDOL Solution for Injection will be injected slowly usually into a blood vessel under the surface of the arm or injected into muscle (usually the buttocks) or under the skin. Alternatively, ZYDOL Solution for Injection will be diluted and infused into a vein.

How long should you receive ZYDOL Solution for Injection?

Your prescriber should have discussed with you, how long the course of injections will last. They will arrange a plan for stopping treatment. This will outline how to gradually reduce the dose and stop taking the medicine.

If you receive more ZYDOL Solution for Injection than you should

If you have received an additional dose by mistake, this will generally have no negative effects. You should receive your next dose as prescribed.

If you (or someone else) received a very high dose of ZYDOL Solution for Injection you should go to hospital or call a doctor straight away. Signs of an overdose include very small pupils, being sick, fall in blood pressure, fast heartbeat, collapse, unconsciousness, fits and breathing difficulties or shallow breathing.

If you miss a dose of ZYDOL Solution for Injection

If you do not receive your ZYDOL Solution for Injection or infusion, pain is likely to return. You should not receive a double dose to make up for forgotten individual doses, simply continue receiving ZYDOL Solution for Injection as before.

If you stop receiving ZYDOL Solution for Injection

Do not suddenly stop taking this medicine. If you want to stop taking this medicine, discuss this with your prescriber first. They will tell you how to do this, usually by reducing the dose gradually so that any unpleasant withdrawal effects are kept to a minimum.

Withdrawal symptoms such as restlessness, difficulty sleeping, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increased blood pressure, feeling or being

sick, diarrhoea, shaking, shivering or sweating may occur if you suddenly stop taking this medicine.

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

4. POSSIBLE SIDE EFFECTS

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

You should see a doctor immediately if you experience symptoms of an allergic reaction such as swollen face, tongue and/or throat, and/or difficulty swallowing or hives together with difficulties in breathing.

The most common side effects during treatment with ZYDOL Solution for Injection are nausea and dizziness, which occur in more than 1 in 10 people.

Very common: may affect more than 1 in 10 people

- dizziness
- feeling sick (nausea)

Common: may affect up to 1 in 10 people

- headaches, drowsiness
- fatigue
- constipation, dry mouth, being sick (vomiting)
- sweating (hyperhidrosis)

Uncommon: may affect up to 1 in 100 people

- effects on the heart and blood circulation (pounding of the heart, fast heartbeat, feeling faint or collapse). These adverse effects may particularly occur in patients in an upright position or under physical strain.
- urge to be sick (retching), stomach trouble (e.g. feeling of pressure in the stomach, bloating), diarrhoea
- skin reactions (e.g. itching, rash)

Rare: may affect up to 1 in 1,000 people

- allergic reactions (e.g. difficulty in breathing, wheezing, swelling of skin) and shock (sudden circulation failure) have occurred in very rare cases.
- slow heartbeat
- increase in blood pressure
- abnormal sensations (e.g. itching, tingling, numbness), trembling, epileptic fits, muscle twitches, uncoordinated movement, transient loss of consciousness (syncope), speech disorders.
- Epileptic fits have occurred mainly at high doses of tramadol or when tramadol was taken at the same time as other medicines which may induce fits.
- changes in appetite
- hallucination, confusional state, sleep disorders, delirium, anxiety and nightmares

- Psychological complaints may appear after treatment with ZYDOL Solution for Injection. Their intensity and nature may vary (according to the patient's personality and length of therapy). These may appear as a change in mood (mostly high spirits, occasionally irritated mood), changes in activity (usually suppression, occasionally increase) and decreased cognitive and sensory perception (changes in senses and recognition, which may lead to errors in judgment).
- blurred vision, excessive dilation of the pupils (mydriasis), constriction of the pupils (miosis)
- slow breathing, shortness of breath (dyspnoea)
- Worsening of asthma has been reported, however it has not been established whether it was caused by tramadol. If the recommended doses are exceeded, or if other medicines that depress brain function are taken at the same time, breathing may slow down.
- weak muscles
- passing urine with difficulty or pain, passing less urine than normal (dysuria).

Very rare: may affect up to 1 in 10,000 people

- increase in liver enzyme values

Not known: frequency cannot be estimated from the available data

- decrease in blood sugar level
- hiccups

dependence and addiction (see section 'How do I know if I am addicted')

Serotonin syndrome, that can manifest as mental status changes (e.g. agitation, hallucinations, coma), and other effects, such as fever, increase in heart rate, unstable blood pressure, involuntary twitching, muscular rigidity, lack of coordination and/or gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea) (see section 2 'What you need to know before you take ZYDOL Solution for Injection').

Drug Withdrawal

When you stop receiving ZYDOL Solution for Injection, you may experience drug withdrawal symptoms, which include restlessness, difficulty sleeping, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increased blood pressure, feeling or being sick, diarrhoea, shaking, shivering or sweating

How do I know if I am addicted?

If you notice any of the following signs whilst taking ZYDOL Solution for Injection, it could be a sign that you have become addicted.

- You need to take the medicine for longer than advised by your prescriber
- You feel you need to use more than the recommended dose
- You are using the medicine for reasons other than prescribed
- When you stop taking the medicine you feel unwell, and you feel better once taking the medicine again

If you notice any of these signs, it is important you talk to your prescriber.

Reporting of side effects

If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: 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 ZYDOL Solution for Injection

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the label. The expiry date refers to the last day of that month. Do not store above 30°C.

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 protect the environment.

6. Contents of the pack and other information

What ZYDOL Solution for Injection contains

The active substance is tramadol hydrochloride.

The other ingredients are: sodium acetate and water for injection

What ZYDOL Solution for Injection looks like and contents of the pack

ZYDOL Solution for Injection is a clear colourless solution.

ZYDOL Solution for Injection is supplied in boxes of five ampoules, each containing 2 ml solution.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

Grünenthal Ltd.

1 Stokenchurch Business Park

Ibstone Road

Stokenchurch

England

HP14 3FE

UK

Manufacturer:

Grünenthal GmbH

Zieglerstr. 6

D-52078

Germany

Other formats:

To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge:

0800 198 5000 (UK Only)

Please be ready to give the following information:

Product name	Reference number
ZYDOL SOLUTION FOR INJECTION	PL 21727/0002

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