

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

^NZYTRAM XL®

Tramadol Hydrochloride Controlled Release Tablets

Read this carefully before you start taking **ZYTRAM XL** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ZYTRAM XL**.

Serious Warnings and Precautions

- Even if you take ZYTRAM XL as prescribed you are at a risk for opioid addiction, abuse and misuse. This can lead to overdose and death. To understand your risk of opioid addiction, abuse, and misuse you should speak to your prescriber (e.g., doctor).
- When you take ZYTRAM XL tablets they must be swallowed whole. Do not cut, break, crush, chew, or dissolve the tablet. This can be dangerous and can lead to death or seriously harm you.
- Life-threatening breathing problems can happen while taking ZYTRAM XL, especially if not taken as directed. Babies are at risk of life-threatening breathing problems if their mothers take opioids while pregnant or nursing.
- Never give anyone your ZYTRAM XL. They could die from taking it. If a person has not been prescribed ZYTRAM XL, taking even one dose can cause a fatal overdose. This is especially true for children.
- If you took ZYTRAM XL while you were pregnant, whether for short or long periods of time or in small or large doses, your baby can suffer life-threatening withdrawal symptoms after birth. This can occur in the days after birth and for up to 4 weeks after delivery. If your baby has any of the following symptoms:
 - has changes in their breathing (such as weak, difficult or fast breathing)
 - is unusually difficult to comfort
 - has tremors (shakiness)
 - has increased stools, sneezing, yawning, vomiting, or fever

Seek immediate medical help for your baby.

- Taking ZYTRAM XL with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death.

What is ZYTRAM XL used for?

ZYTRAM XL is used in adults to manage moderate to moderately severe pain. It is used when continuous treatment is required for several days or more.

How does ZYTRAM XL work?

ZYTRAM XL is a painkiller belonging to the class of drugs known as opioids. It relieves pain by acting on specific nerve cells of the spinal cord and brain.

What are the ingredients in ZYTRAM XL?

Medicinal ingredients: tramadol hydrochloride

Non-medicinal ingredients: hydrogenated vegetable oil, hypromellose, lactose, magnesium stearate, polyethylene glycol, talc, titanium dioxide. The 75 mg tablets also contain iron oxide and FD&C Blue No. 2

ZYTRAM XL comes in the following dosage forms:

Controlled Release Tablets: 75 mg, 100 mg, 150 mg, 200 mg, 300 mg, and 400 mg

Do not use ZYTRAM XL if:

- your healthcare professional did not prescribe it for you
- you are allergic to tramadol, other opioids, or any of the other ingredients in ZYTRAM XL
- your pain can be controlled by the occasional use of painkillers including those available without a prescription
- you have severe asthma, trouble breathing, or other breathing problems
- you have any heart problems
- you have bowel blockage or narrowing of the stomach or intestines
- you have severe pain in your abdomen
- you have increased pressure in your skull or have a head injury
- you have or have a history of epilepsy
- you have severe liver problems
- you have severe kidney problems
- you suffer from alcoholism or alcohol withdrawal
- you are taking or have taken within the past 2 weeks a Monoamine Oxidase Inhibitor (MAOI) (such as phenelzine sulfate, tranylcypromine sulfate, moclobemide or selegiline)
- you are less than 18 years old and having (or recently had) your tonsils or adenoids removed because of frequent interruption of breathing during sleep
- you are less than 12 years old
- you are pregnant or planning to become pregnant or you are in labour or delivery.
- you are breastfeeding or plan to breastfeed.
- you have recently taken alcohol, hypnotics, centrally acting analgesics, opioids, or psychotropic drugs. Ask your healthcare professional if you are unsure
- you are going to have, or recently had, a planned surgery

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ZYTRAM XL. Talk about any health conditions or problems you may have, including if you:

- have a history of illicit or prescription drug or alcohol abuse
- have low blood pressure
- have past or current depression
- suffer from chronic or severe constipation
- have been told that you metabolize tramadol or other pain medications rapidly
- have problems with your thyroid, adrenal or prostate gland

- have diabetes
- have liver problems
- have kidney problems
- have or have had problems with your mood (such as depression or anxiety), hallucinations, or other mental health problems
- have a central nervous system (CNS) infection
- are dependent on opioids
- are planning on drinking alcohol, drinking alcohol while taking ZYTRAM XL may cause dangerous side effects, including death. Do not drink alcohol while taking ZYTRAM XL.
- have suicidal thoughts or actions
- have circulatory problems (e.g., body does not get enough oxygen and nutrients to function properly due to a lack of blood flow)
- have been told you are at risk of having heart problems, hyponatremia (low sodium levels in the blood), or seizures
- have a condition that causes weakness or frailty
- have difficulty urinating
- have a sleep disorder which causes pauses in breathing or shallow breathing while sleeping (sleep apnea)
- are over 65 years of age

Other warnings you should know about:

Taking ZYTRAM XL can cause the following serious side effects:

- **Allergic reactions:** Serious and rarely fatal allergic reactions (e.g., swelling of lips and throat, blistering of skin and/or lips or neck) have been reported in patients receiving therapy with tramadol. Seek medical attention immediately.
- **Disorder of the adrenal gland:** You may develop a disorder of the adrenal gland called adrenal insufficiency. This means that your adrenal gland is not making enough of certain hormones. You may experience symptoms such as:
 - nausea, vomiting
 - feeling tired, weak or dizzy
 - decreased appetite

You may be more likely to have problems with your adrenal gland if you have been taking opioids for longer than one month. Your healthcare professional may do tests, give you another medication, and slowly take you off ZYTRAM XL.

- **Hypoglycemia** (low blood sugar): ZYTRAM XL can decrease your blood sugar levels. Diabetic patients may need to monitor their blood sugar more often. If you notice changes, discuss this with your healthcare professional.
- **Seizure risk:** Seizures have been experienced by patients taking ZYTRAM XL at the doses prescribed. This risk may increase with higher doses.
- **Serotonin toxicity (also known as Serotonin Syndrome):** ZYTRAM XL can cause serotonin toxicity, a rare but potentially life-threatening condition. It can cause serious changes in how your brain, muscles and digestive system work. You may develop serotonin toxicity if you take ZYTRAM XL with certain anti-depressants or migraine medications. Serotonin toxicity symptoms include:
 - fever, sweating, shivering, diarrhea, nausea, vomiting;
 - muscle shakes, jerks, twitches or stiffness, overactive reflexes, loss of coordination;
 - fast heartbeat, changes in blood pressure;

- confusion, agitation, restlessness, hallucinations, mood changes, unconsciousness, and coma.
- **Sleep apnea:** Opioids can cause a problem called sleep apnea (stopping breathing from time to time while sleeping). Tell your healthcare professional if you have a history of sleep apnea or if anyone notices that you stop breathing from time to time while sleeping.

See the **Serious side effects and what to do about them** table below for more information on these and other serious side effects.

Adolescents (12 to 18 years old): You should not use ZYTRAM XL if your child:

- is overweight (obese)
- has obstructive sleep apnea (a condition where your breathing starts and stops while you sleep)
- has severe lung disease

There is a higher risk of serious breathing problems if your child takes ZYTRAM XL and has any of the above conditions.

Driving and using machines: Before you do tasks which may require special attention, you should wait until you know how you react to ZYTRAM XL. ZYTRAM XL can cause:

- drowsiness
- dizziness or
- light headedness

This can usually occur after you take your first dose and when your dose is increased.

Elimination: You may see tablets in your stools (bowel movements) or in your colostomy, when using ZYTRAM XL. Do not be concerned, the medication has already been released.

Opioid dependence and addiction: There are important differences between physical dependence and addiction. It is important that you talk to your healthcare professional if you have questions or concerns about abuse, addiction or physical dependence.

Pregnancy, nursing, labour and delivery: Do not use ZYTRAM XL while pregnant, nursing, during labour or delivery. Opioids can be transferred to your baby through breast milk, or while still in the womb. ZYTRAM XL can then cause life-threatening breathing problems in your unborn baby or nursing infant.

If you are pregnant and are taking ZYTRAM XL, it is important that you don't stop taking your medication all of a sudden. If you do, it can cause a miscarriage or a still-birth. Your healthcare professional will monitor and guide you on how to slowly stop taking ZYTRAM XL. This may help avoid serious harm to your unborn baby.

Sexual function and reproduction: Long term use of opioids may lead to a decrease in sex hormone levels. It may also lead to low libido (desire to have sex), erectile dysfunction or being infertile.

Testing and check-ups:

- ZYTRAM XL can cause abnormal blood test results including decreased blood sugar. Your healthcare professional will decide when to perform blood tests and will interpret the results.
- Your healthcare professional will also regularly monitor you for signs of misuse and abuse.

Worsening pain: Taking opioids for pain can sometimes have the unintended effect of making your pain feel worse (opioid-induced hyperalgesia) even though your opioid dose has been unchanged or increased. This can also include feeling pain in new places in your body, or feeling pain from something that would not normally hurt, for example, feeling pain from clothing touching your skin. Tell your healthcare professional if you notice a change like this in your pain while you are taking ZYTRAM XL.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Serious Drug Interactions

Serious drug interactions with ZYTRAM XL include:

- benzodiazepines used to help you sleep or that help reduce anxiety.
- central nervous system (CNS) depressants used to slow down the nervous system. These can include:
 - other opioids used to relieve pain (e.g., methadone);
 - hypnotics used to help with sleeping;
 - antidepressants used for depression and mood disorders (e.g., fluoxetine, citalopram, venlafaxine; tricyclic antidepressants such as amitriptyline, imipramine, maprotiline, paroxetine; serotonin norepinephrine re-uptake inhibitors [SNRIs]; and selective serotonin re-uptake inhibitors [SSRIs] such as St. John's Wort);
 - anxiolytics, tranquilizers, and phenothiazines used to treat mental or emotional disorders;
 - muscle relaxants used to treat muscle spasms and back pain (e.g., baclofen);
 - medicines known as "gabapentinoids" (e.g., pregabalin);
 - general anaesthetics used during surgery;
 - antipsychotics and neuroleptics used to treat mental health disorders (e.g., chlorpromazine, pimozide, haloperidol, droperidol, ziprasidone, and risperidone);
 - antihistamines used to treat allergies;
 - antiemetics used to prevent nausea or vomiting (e.g., domperidone and ondansetron);
 - sedatives which may enhance the drowsiness;
 - beta blockers used to lower blood pressure;
 - alcohol. This includes prescription and non-prescription medications that contain alcohol. Do not drink alcohol while you are taking ZYTRAM XL. It can lead to drowsiness, unusually slow or weak breathing, serious side effects, or a fatal overdose.
- monoamine oxidase inhibitors (MAOIs) used to treat depression. Do not take ZYTRAM XL with MAOIs or if you have taken MAOIs in the last 14 days.

The following may interact with ZYTRAM XL:

- anticoagulants used to thin the blood and prevent blood clots (e.g., warfarin and coumadin)
- anti-retrovirals used to treat viral infections (e.g., ritonavir)
- anti-fungals used to treat fungal infections (e.g., ketoconazole, fluconazole, and voriconazole)
- antibiotics used to treat bacterial infections (e.g., rifampin, erythromycin, clarithromycin, azithromycin, tacrolimus, moxifloxacin, levofloxacin, ciprofloxacin, and pentamidine)
- heart medications (e.g., digoxin, quinidine, procainamide, disopyramide, amiodarone, sotalol,

ibutilide, dronedarone, flecainide, propafenone, sunitinib, nilotinib, ceritinib, vandetanib, salmeterol and formoterol))

- antimalarials used to treat malaria (e.g., quinine and chloroquine)
- medicines used to treat cancer (e.g., vorinostat and arsenic trioxide)
- grapefruit juice
- medicines used to decrease electrolyte levels in the body (e.g., diuretics, laxatives, enemas, amphotericin B, high doses of corticosteroids, and proton pump inhibitors)
- carbamazepine, used to treat certain types of seizures

If you are unsure about the medications you are taking, ask your healthcare professional.

How to take ZYTRAM XL:

- ZYTRAM XL must be taken orally, by mouth.
- Take ZYTRAM XL every 24 hours as prescribed, with a glass of water. It can be taken with or without food.
- **Swallow whole. Do not cut, break, crush, chew or dissolve the tablet. This can be dangerous and can lead to death or seriously harm you.**
- Review your pain regularly with your healthcare professional to determine if you still need ZYTRAM XL. Be sure to use ZYTRAM XL only for the condition for which it was prescribed.

Usual dose:

Your dose is tailored/personalized just for you. Take it exactly as your healthcare professional has told you to. Do not increase or decrease your dose without consulting your healthcare professional. Taking higher doses can lead to more side effects and a greater chance of overdose.

The usual starting dose of ZYTRAM XL is 150 mg per day.

You should not take more than the maximum recommended dose of 400 mg of ZYTRAM XL per day.

Exceeding this recommendation can result in respiratory depression (shallow, slow breathing), seizures, coma, heart stoppage and death.

Stopping your Medication: If you have been taking ZYTRAM XL for more than a few days you should not stop taking it all of a sudden. You should check with your healthcare professional for directions on how to slowly stop taking it. You should do it slowly to avoid uncomfortable symptoms such as having:

- body aches
- diarrhea
- goosebumps
- loss of appetite
- nausea
- feeling nervous or restless
- runny nose
- sneezing
- tremors or shivering
- stomach cramps
- rapid heart rate (tachycardia)
- having trouble sleeping
- an unusual increase in sweating

- an unexplained fever
- weakness
- yawning

By reducing or stopping your opioid treatment, your body will become less used to opioids. If you start treatment again, you will need to start at the lowest dose. You may overdose if you restart at the last dose you took before you slowly stopped taking ZYTRAM XL.

Refilling your Prescription for ZYTRAM XL: A new written prescription is required from your healthcare professional each time you need more ZYTRAM XL. Therefore, it is important that you contact your healthcare professional before your current supply runs out.

Only obtain prescriptions for this medicine from the healthcare professional in charge of your treatment. Do not seek prescriptions from other healthcare professionals unless you switch to another healthcare professional for your pain management.

Overdose:

Signs of an overdose with ZYTRAM XL may include:

- unusually slow or weak breathing
- dizziness
- confusion
- extreme drowsiness
- fits (seizures)
- irritation and discomfort in the stomach and gut
- nausea
- vomiting
- feeling unwell
- pale color and sweating
- toxic leukoencephalopathy (a brain disorder affecting the brain's white matter)
- QT prolongation (abnormal electrical activity in the heart)
- lack of muscle shape and tone
- cold and clammy skin
- shrinking of pupils
- slow heart rate
- low blood pressure

If you think you, or a person you are caring for, have taken too much ZYTRAM XL, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

It is very important that you do not miss any doses. If you miss one dose, skip the missed dose and take your next dose as scheduled. Do not take two doses at once to make up for a missed dose. If you miss several doses in a row, talk to your healthcare professional before restarting your medication.

What are possible side effects from using ZYTRAM XL?

These are not all the possible side effects you may have when taking ZYTRAM XL. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- drowsiness
- insomnia
- dizziness
- fainting
- nausea, vomiting, or a poor appetite
- dry mouth
- headache
- problems with vision
- weakness, uncoordinated muscle movement
- itching
- sweating
- hiccups
- increased sensitivity to feeling pain
- constipation; talk with your healthcare professional about ways to prevent constipation when you start using ZYTRAM XL
- low sex drive, impotence (erectile dysfunction), infertility

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
UNCOMMON			
Seizures (fits): uncontrollable shaking with or without loss of consciousness			✓
RARE			
Hallucinations: seeing or hearing things that are not there			✓
Overdose: hallucinations, confusion, inability to walk normally, slow or weak breathing, extreme sleepiness, sedation, or dizziness, floppy muscles/low muscle tone, cold and clammy skin			✓
Respiratory depression: slow, shallow or weak breathing			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Allergic reaction: rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			✓
Bowel blockage (impaction): abdominal pain, severe constipation, nausea			✓
Withdrawal: nausea, vomiting, diarrhea, anxiety, shivering, cold and clammy skin, body aches, loss of appetite, sweating		✓	
Fast, slow or irregular heartbeat: heart palpitations		✓	
Hypotension (low blood pressure): dizziness, fainting, light-headedness	✓		
Serotonin toxicity (also known as serotonin syndrome): a reaction which may cause feelings of agitation or restlessness, flushing, muscle twitching, involuntary eye movements, heavy sweating, high body temperature (>38°C), or rigid muscles			✓
VERY RARE			
Hypoglycemia (decreased blood sugar): dizziness, lack of energy, drowsiness, headache, trembling, sweating			✓
UNKNOWN FREQUENCY			
Disorders of the adrenal gland: nausea, vomiting, anorexia, fatigue, weakness, dizziness, or low blood pressure			✓
Sleep apnea: stop breathing for short periods during your normal nightly sleep		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store tablets at room temperature (15°C - 30°C). Protect from light, moisture and high humidity.
- Keep unused or expired ZYTRAM XL in a secure place to prevent theft, misuse or accidental exposure.
- Keep ZYTRAM XL under lock, out of sight and reach of children and pets.
- Never take medicine in front of small children as they will want to copy you. Accidental ingestion by a child is dangerous and may result in death. If a child accidentally takes ZYTRAM XL, get emergency help right away.
- ZYTRAM XL should never be thrown into household trash, where children and pets may find it. It should be returned to a pharmacy for proper disposal.

If you want more information about ZYTRAM XL:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>; the manufacturer's website <http://www.purdue.ca>, or by calling 1-800-387-4501.

This leaflet was prepared by Purdue Pharma

Last Revised: December 01, 2023