

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

^NZYTRAM XL[®]
Tramadol 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 feverSeek 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 a medicine used to manage your pain.

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. It contains tramadol, a medicine used to treat moderate to moderately severe pain and should relieve your pain and help the pain relief last longer.

Your pain may increase or decrease from time to time and your doctor may need to change the amount of tramadol you take daily (daily dosage).

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:

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

Do not use ZYTRAM XL if:

- your doctor 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 a head injury
- you are at risk for seizures
- you have severe liver disease
- you have severe kidney disease
- you suffer from alcoholism
- you are taking or have taken within the past 2 weeks a Monoamine Oxidase Inhibitor (MAO) (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
- you are breastfeeding

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 had seizures (convulsions)
- have a condition that may put you at increased risk of seizures (epilepsy)
- central nervous system (CNS) infection
- have low blood pressure
- have a history of sleep apnea

- have past or current depression
- suffer from chronic or severe constipation
- have been told that you metabolize tramadol or other pain medications rapidly
- have diabetes
- you had surgery within the last 12 -24 hours
- you have a planned surgery within the next 24 hours
- have problems with your thyroid, adrenal or prostate gland
- have or had in the past hallucinations or other severe mental problems
- suffer from migraines
- are over 65 years of age
- are planning to become pregnant

Other warnings you should know about:

Seizures have been experienced by patients taking ZYTRAM XL at the doses prescribed. This risk may increase with higher doses.

Alcohol

You must not consume alcohol while taking ZYTRAM XL tablets, as it may increase the chance of experiencing dangerous side effects. Also, you should tell your doctor if you drink alcohol regularly or have a history of alcoholism.

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 doctor.

Opioid dependence and addiction

There are important differences between physical dependence and addiction. It is important that you talk to your doctor 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 doctor will monitor and guide you on how to slowly stop taking ZYTRAM XL. This may help avoid serious harm to your unborn baby.

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.

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.

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.

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 doctor may do tests, give you another medication, and slowly take you off ZYTRAM XL.

Serotonin Syndrome

ZYTRAM XL can cause serotonin syndrome, 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 syndrome if you take ZYTRAM XL with certain anti-depressants or migraine medications.

Serotonin syndrome 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.

Sexual Function/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.

Sleep apnea

Opioids can cause a problem called sleep apnea (stopping breathing from time to time while sleeping). Tell your doctor if you have a history of sleep apnea or if anyone notices that you stop breathing from time to time while sleeping.

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.

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

The following may interact with ZYTRAM XL:

- 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
- other opioid analgesics (for pain)
- general anesthetics (used during surgery)
- drugs used to help you sleep or that help reduce anxiety (benzodiazepines)
- antidepressants (for depression and mood disorders). **Do not** take ZYTRAM XL with monoamine oxidase inhibitors (MAOI) or if you have taken MAO's in the last 14 days before treatment with ZYTRAM XL
- drugs used to treat serious mental or emotional disorders (such as schizophrenia)
- antihistamines (for allergies)
- anti-emetics (for the prevention of vomiting)
- drugs used to treat muscle spasms and back pain
- anticoagulants (blood thinners)
- anticonvulsant drugs (for epilepsy)
- anti-retroviral drugs (to treat viral infections)
- anti-fungal drugs (for fungal infections)
- antibiotic drugs (for bacterial infections)
- heart medications (e.g. digoxin, quinidine)
- drugs used to treat migraines (e.g. triptans)
- St. John's Wort

How to take ZYTRAM XL:

Take ZYTRAM XL tablets regularly every 24 hours, with or without food, with a full glass of water.

ZYTRAM XL is not recommended for rectal administration.

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.

Usual dose: Your dose is tailored/personalized just for you. Be sure to follow your doctor's dosing instructions exactly. Do not increase or decrease your dose without consulting your doctor. Taking higher doses can lead to more side effects and a greater chance of overdose.

Review your pain regularly with your doctor to determine if you still need ZYTRAM XL. Be sure to use ZYTRAM XL only for the condition for which it was prescribed.

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.

If your pain increases or you develop any side effect as a result of taking ZYTRAM XL, tell your doctor immediately.

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 doctor 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 doctor each time you need more ZYTRAM XL. Therefore, it is important that you contact your doctor before your current supply runs out.

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

Overdose:

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

Signs of overdose may include:

- unusually slow or weak breathing
- dizziness
- confusion
- extreme drowsiness
- fits (seizures)
- irritation and discomfort in the stomach and gut
- loss of appetite
- nausea
- vomiting
- feeling unwell
- unusually pale color and sweating

Cases of abnormal electrical conduction in the heart (QT prolongation) have been reported.

Missed Dose:

If you miss one dose, take it as soon as possible. However, if it is almost time for your next dose, then skip the missed dose. Do not take two doses at once. If you miss several doses in succession, talk to your doctor before restarting your medication.

What are possible side effects from using ZYTRAM XL?

These are not all the possible side effects you may feel when taking ZYTRAM XL. If you experience any side effects not listed here, contact 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
- constipation
- low sex drive, impotence (erectile dysfunction), infertility

Talk with your doctor or pharmacist about ways to prevent constipation when you start using ZYTRAM XL.

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	
RARE			
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			✓
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		✓	
Low Blood Pressure: dizziness, fainting, light-headedness	✓		
Serotonin Syndrome: agitation or restlessness, loss of muscle control or muscle twitching, tremor, diarrhea.			✓
VERY RARE			
Decreased Blood Sugar (hypoglycemia): dizziness, lack of energy, drowsiness, headache, trembling, sweating			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to 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/drug.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 health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- **Keep unused or expired ZYTRAM XL in a secure place to prevent theft, misuse or accidental exposure.**
- Store tablets at room temperature (15°C - 30°C). Keep in a dry place.
- **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.**

Disposal:

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 www.purdue.ca, or by calling 1-800-387-4501.

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