

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

AMBIEN CR 6.25 mg

AMBIEN CR 12.5 mg

Extended-Release Tablets

Active ingredient and its quantity:

Each Ambien CR 6.25 mg tablet contains: Zolpidem Tartrate 6.25 mg

Each Ambien CR 12.5 mg tablet contains: Zolpidem Tartrate 12.5 mg

Inactive and allergenic ingredients in the preparation – see Section 2 “Important information about some of the ingredients of the medicine” and Section 6 “Further information”.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

The medicine is intended for the treatment of insomnia characterized by difficulties with sleep onset and/or sleep maintenance.

Therapeutic group: Hypnotic and sedative substances.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You have ever experienced complex sleep behavior (such as driving a car, making and eating food, talking on the phone or having sex while not being fully awake) after taking Ambien CR (see “Special warnings regarding use of the medicine”).
- You are sensitive (allergic) to the active ingredient in the medicine (zolpidem) or to any of the additional ingredients contained in the medicine (see section 6).
- You have had in the past an allergic reaction to zolpidem-containing medicines. Symptoms of serious allergic reaction to zolpidem may include: swelling of your face, lips and throat that may cause difficulty in breathing or swallowing.
- You are suffering from severe liver failure.
- You drank alcohol in the evening or before bed.
- You will not be able to get a full night's sleep after taking the medicine (7-8 hours) before you need to be active again.

Special warnings regarding use of the medicine:

Do not take more Ambien CR than prescribed.

Take Ambien CR just before bedtime; Do not use the medicine for more than four consecutive weeks!; Refer to a doctor if you think the effect of the medicine has declined. Do not increase the dosage on your own; Similar to other hypnotic preparations, use of Ambien CR may cause dependence. The risk for this increases with prolonged use; As with other hypnotic preparations uncontrolled discontinuation of treatment can be rarely accompanied by withdrawal effects, e.g., muscle and stomach cramps, tremor, recurrence of insomnia, vomiting, nausea, sweating, seizures, confusion (delirium); **Ambien CR may cause serious side effects, including complex sleep behavior.**

After taking Ambien CR, you may get out of bed when you are not fully awake and engage in activities that you are not aware that you are doing. The next morning, you may not remember that you did anything during the night. These activities can occur with Ambien CR, whether or not you drink alcohol or take other medicines that make you sleepy. Some of these behaviors you are unaware of have caused serious injuries and death.

People taking Ambien CR have reported: sleepwalking; driving a car while sleeping (“sleep-driving”); making and eating food; talking on the phone; having sex

Stop taking Ambien CR and report to the doctor immediately if you find out that you have done any of the activities described above after taking Ambien CR.

Store Ambien CR in a safe place to avoid incorrect use or abuse. Tell your doctor if you have abused or developed a dependency on alcohol, prescription medicines or drugs in the past; If an acute allergic reaction to the medicine develops, manifested by angioedema [edema of the tongue, glottis (the opening to the trachea), larynx (the voice box)], do not use this medicine again; As this medicine impairs alertness, patients, especially the elderly, are at a higher risk of falling; A reduced dosage (6.25 mg) is advisable in the elderly, in women and in patients with liver function problems; see section 3; Use of Ambien CR together with other medicines possessing a sedative effect (e.g., medicines from the benzodiazepine group, opioids, certain antidepressants, alcohol), including daytime use, increases the risk of depression of the central nervous system. If Ambien CR is taken concomitantly with these medicines, the attending doctor must consider adjusting the dosage of the medicines. Do not take Ambien CR together with medicines possessing a hypnotic sedative effect (including other zolpidem-containing medicines) before going to sleep or at night, unless your doctor has instructed you to do so; The risk of psychomotor impairment in the morning after taking Ambien CR, including impaired ability to drive, increases if the medicine is taken at bedtime, without the possibility of 7-8 hours of sleep, if a dosage higher than that recommended by the doctor is taken, if taken in combination with other central nervous system depressants or alcohol, or if taken in combination with other medicines that may increase the levels of zolpidem in the blood; Ambien CR may cause drowsiness and decreased level of alertness, which may cause falls, and, as a result, even lead to severe injuries. There have been reports of severe injuries such as hip fractures and

intracranial hemorrhage; While taking Ambien CR, do not drink alcohol or take opioids or other medicines that may cause you to be sleepy or dizzy without first consulting the doctor. When Ambien CR is taken together with alcohol or other medicines that cause sleepiness or dizziness, it may significantly worsen your sleepiness and dizziness.

Before treatment with the medicine, tell the doctor if:

You have a history of depression, mental illnesses, or suicidal thoughts or actions; You have a history of alcohol or drug abuse or addiction; You are suffering from a kidney or liver disease; You have a lung disease or breathing problems; You have sleep apnea; You have a muscle disease called myasthenia gravis; You are pregnant, planning a pregnancy, breastfeeding or planning to breastfeed (see “Pregnancy, breastfeeding and fertility”).

Children and adolescents:

The tablets are not recommended for treatment of children and adolescents under 18 years of age since the effectiveness and safety of use of the medicine in these ages have not been proven.

Drug interactions:

Ambien CR and other medicines might interact with each other causing serious side effects (see section “Special warning regarding use of this medicine”). Ambien CR may affect the way other medicines work, and other medicines may affect the way Ambien CR works.

If you are taking, or have recently taken, or plan to take, other medicines, including non-prescription medicines or nutritional supplements, tell the doctor or pharmacist. In particular, inform the doctor or pharmacist if you are:

taking benzodiazepines; taking opioids as it may increase the risk of breathing problems (respiratory depression); taking tricyclic antidepressants; taking other medicines that can make you sleepy or affect your breathing (including other zolpidem-containing medicines); drinking alcohol.

Sertraline, fluoxetine, fluvoxamine – antidepressants; Chlorpromazine, haloperidol – for treatment of mental illnesses; St. John's wort (*Hypericum*); Rifampin, ciprofloxacin – for treatment of infections; Ketoconazole – for treatment of fungi.

You can ask your pharmacist for a list of medicines that interact with Ambien CR. Know the medicines you are taking. Keep a list of your medicines to show your doctor and pharmacist when you receive a new medicine.

Use of the medicine and food

Do not take the medicine with or immediately after a meal. Ambien CR may help you fall asleep faster if it is taken on an empty stomach.

Use of the medicine and alcohol consumption

Do not drink wine or alcoholic beverages during the course of treatment with the medicine.

Pregnancy, breastfeeding and fertility

If you are pregnant or planning a pregnancy, consult a doctor before using the medicine. Use of Ambien CR in the third trimester of pregnancy may harm the unborn baby.

Tell your doctor if you become pregnant or plan to become pregnant during treatment with Ambien CR.

Babies born to women who took Ambien CR during the third trimester of pregnancy may develop symptoms of breathing problems and sedation (such as sleepiness or low muscle tone).

If you are breastfeeding or plan to breastfeed, consult a doctor before using the medicine. Ambien CR passes into your breast milk. Consult a doctor about the best way to feed your baby while you use Ambien CR.

Driving and operating machinery

Use of this medicine may impair alertness and therefore requires caution when driving a car, operating dangerous machinery and when engaging in any activity which requires alertness. Do not drive, operate dangerous machinery or engage in other dangerous activities until you know how Ambien CR affects you.

The medicine may affect your ability to concentrate on the day after you take the medicine, even if you feel completely alert.

The risk of a psychomotor disturbance, including impaired ability to drive, increases if the medicine is taken at bedtime, without the possibility of 7-8 hours of sleep, if a dosage higher than that recommended by the doctor is taken, if taken in combination with other central nervous system depressants or alcohol, or if taken in combination with other medicines that may increase zolpidem levels in the blood.

Those who drive a car and those who operate machinery must know that as with other hypnotics (sleep medicines), there may be a potential risk of side effects, including drowsiness, prolonged response time, dizziness, sleepiness, blurred/double vision, reduced alertness and impaired driving the morning after treatment. To reduce the risk, it is recommended to get a full night of sleep (7-8 hours).

Important information about some of the ingredients of the medicine

The medicine contains **lactose**. Consult your doctor before starting use of the medicine if you suffer from intolerance to certain sugars.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

The dosage and the treatment regimen will be determined by the doctor only.

The usual dosage is generally:

If needed, take only one Ambien CR tablet at night, immediately before bedtime.

The usual initial dosage is generally: For women – one tablet of 6.25 mg. For men – 6.25-12.5 mg.

In the elderly and patients with liver function problems, the dosage is one 6.25 mg



tablet, once at nighttime, immediately before bedtime. Do not use if severe liver failure has been diagnosed.

Do not exceed a dosage of 12.5 mg, once a day, immediately before bedtime.

Make sure that you can sleep at least 7-8 hours after taking the medicine.

Do not exceed the recommended dose.

Do not take Ambien CR if you drank alcohol on the same evening or before bedtime. Do not take Ambien CR with or immediately after a meal. Ambien CR can help you fall asleep faster if you take it on an empty stomach.

Treatment duration: The usual duration of treatment with the medicine is two days to four weeks.

In some patients, the higher levels of the medicine in the blood in the morning, after taking 12.5 mg at bedtime, increase the risk of impaired alertness, ability to drive and capacity to concentrate.

Refer to your doctor if your insomnia worsens or does not improve within 7-10 days. This may indicate that there is another medical condition causing your sleep problems. The tablets are not intended for children and adolescents under 18 years of age.

Mode of administration

Swallow the tablet whole. Do not chew, halve or crush the tablet. The tablet is composed of two layers, which release the active ingredient in an extended manner.

Tell the doctor if you cannot swallow the Ambien CR tablet whole. You may need to receive a different medicine.

If you accidentally took a higher dosage, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine:

Take the medicine immediately before going to sleep, only if you can then sleep for at least 7-8 hours. If you forgot to take the medicine at bedtime, do not take a dose at any other time, as you may feel drowsy, dizzy and confused throughout the day.

Do not take a double dose to compensate for the forgotten dose. Take the next dose at the usual time and consult the doctor.

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with Ambien CR without consulting a doctor or pharmacist, and even then, only gradually.

If you stop taking the medicine:

One or two days after stopping the medicine, the following reactions may occur: sleep problems, nausea, flushing, dizziness, uncontrollable crying, vomiting, abdominal cramps, an anxiety attack, nervousness and pain in the stomach area.

Do not take medicines in the dark! Check the label and dose each time you take medicine. Wear glasses if you need them.

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

4. SIDE EFFECTS

As with any medicine, use of Ambien CR may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Ambien CR may cause serious side effects including:

Ambien CR can make you sleepy or dizzy and can slow your thinking and motor skills.

Sleepiness on the day after taking the medicine is common, but can be serious. Because Ambien CR can make you sleepy or dizzy, you are at a higher risk for falls; Getting out of bed when you are not fully awake and performing activities without being aware that you are doing them (see "Special warnings regarding use of the medicine" section); **Severe allergic reactions.** Symptoms include swelling of the tongue or throat, breathing problems, nausea and vomiting. Get emergency medical help if you get these symptoms after taking Ambien CR; **Abnormal thoughts and behaviors.** Symptoms include more outgoing or aggressive behavior than normal, confusion (delirium), acting strangely, agitation, hallucinations, worsening of depression, and suicidal thoughts or actions; **Risk of suicide or worsening of depression.** Worsening of depression, including suicidal thoughts and actions can occur during treatment with medicines like Ambien CR. Refer to your doctor immediately if you develop any thoughts of suicide, dying, or worsening depression during treatment with Ambien CR;

Breathing problems (also see "Before treatment with the medicine, tell the doctor if"): Refer to your doctor or get emergency medical help immediately if you develop breathing problems during treatment with Ambien CR;

Problems with your nervous system caused by severe liver disease (hepatic encephalopathy);

Withdrawal symptoms. You may have withdrawal symptoms if you stop taking Ambien CR suddenly. Withdrawal symptoms can be serious and include stomach and muscle cramps, vomiting, sweating, tremor, seizures, and confusion (delirium). Talk to your doctor about gradually stopping Ambien CR to avoid withdrawal symptoms; Memory loss; Anxiety.

Contact the doctor immediately if any side effects listed above or other side effects that concern you occur while using Ambien CR.

Common side effects (affect more than 1/100 patients):

Headache, sleepiness, dry mouth, weakness, unstable walk (ataxia), confusion, drowsiness, stupor (drugged feeling), euphoria, insomnia, lethargy, lightheadedness, vertigo, diarrhea, dyspepsia, hiccups, sinusitis, double vision, vision disturbances, urinary tract infections.

Uncommon side effects (affect between 1/100 and 1/1000 patients):

Increased sweating, pallor, postural hypotension, fainting, chest pains, edema, falls (which may cause serious injuries), fever, general unwell feeling, trauma, cerebrovascular disorder, hypertension, tachycardia, agitation, decreased cognition, feeling detached, concentration difficulties, speech impairment, emotional lability, hallucinations,

hypoesthesia, illusions, leg muscle cramps, migraine, nervousness, numbness, sleeping (after taking the medicine during the day), speech disorder, dulled senses, tremor, loss of appetite, constipation, swallowing impairment, bloating (flatulence), inflammation in the digestive system, infection, impaired liver function and increased level of enzymes, hyperglycemia, thirst, arthritis, menstrual disorder, vaginal inflammation, bronchitis, cough, breathing difficulties, itch, eye irritation, eye pain, eye inflammation, change in taste, tinnitus, bladder inflammation, urinary incontinence.

Rare side effects (affect less than 1/1000 patients):

Vision disturbances, altered saliva, flushing, glaucoma, hypotension, impotence, increased saliva, tenesmus, allergic reaction, aggravation of allergy, anaphylactic shock, face edema, hot flushes, accelerated blood sedimentation, pain, restless leg syndrome, muscle stiffness, increased tolerance to the medicine, weight decrease, angina pectoris, arrhythmia, arteritis, blood circulation problems, excessive heartbeats, aggravated hypertension, heart attack, phlebitis, varicose veins, pulmonary embolism, pulmonary edema, ventricular tachycardia, gait disturbances, abnormal thoughts, aggressive reaction, apathy, increased appetite, decreased libido, delusions, dementia, change in "self" perception, speech disturbances (dysphasia), strange feeling, movement disorders, hypotonia, hysteria, intoxicated feeling, manic reaction, nerve pain, nerve inflammation, neuropathy (a peripheral nervous system disease), neurotic disturbance, panic attacks, partial paralysis, personality disorders, sleepwalking, suicide attempts, severe muscle cramping, yawning, intestinal inflammation, eructation, esophagospasm, gastritis, hemorrhoids, intestinal obstruction, rectal hemorrhage, dental caries, anemia, hyperhemoglobinemia, leukopenia, enlarged lymph node, macrocytic anemia, spot-shaped rash, thrombosis, abscess, herpes, herpes zoster, middle or outer ear infection, increased bilirubin levels, increased liver enzyme levels, gout, hypercholesterolemia or hyperlipidemia, kidney function disorders, periorbital edema, joint disease, muscle weakness, pain radiating to the leg, tendinitis, breast tumors, breast pains, bronchospasm, respiratory depression, nosebleed, reduced blood oxygen, inflammation of the throat, pneumonia, acne, bullous rash, dermatitis, pustular rash, photosensitivity, urticaria, conjunctivitis, corneal ulceration, lacrimation disorder, smell identification disturbance, light flashes, acute renal failure, painful or frequent urination, nocturia, increase in amount of urine, renal inflammation, renal pain, urinary retention.

Side effects of unknown frequency:

Severe liver damage, with or without jaundice, delirium (severe confusion).

Side effects upon discontinuation of the medicine – see details in section 3.

If a side effect occurs, if one of the side effects worsens or persists for more than a few days, or if you suffer from a side effect not mentioned in the leaflet, consult the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. **Do not induce vomiting** unless explicitly instructed to do so by the doctor!

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Storage conditions: Store at a temperature below 30°C.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Ambien CR 6.25 mg: lactose monohydrate 138.913 mg, microcrystalline cellulose, hypromellose, potassium hydrogen tartrate, sodium starch glycolate (type A), magnesium stearate, titanium dioxide, Macrogol 3350, colloidal anhydrous silica, red iron oxide.

Ambien CR 12.5 mg: lactose monohydrate 138.913 mg, microcrystalline cellulose, hypromellose, potassium hydrogen tartrate, sodium starch glycolate (type A), magnesium stearate, titanium dioxide, Macrogol 3350, indigotine (E132)-aluminium lake, colloidal anhydrous silica, yellow iron oxide.

What the medicine looks like and the contents of the package:

Ambien CR 6.25 mg extended-release tablets – round, pink-colored tablets.

Ambien CR 12.5 mg extended-release tablets – round, blue-colored tablets.

Available in packages of 14 or 28 extended-release tablets. Not all package sizes may be marketed.

This leaflet does not contain all the information about the preparation. If you have any question or are not sure about something, please refer to the doctor.

Registration holder and importer's name and address: sanofi-aventis Israel Ltd., P.O.B. 8090 Netanya.

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Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Ambien CR 6.25 mg: 1420531833

Ambien CR 12.5 mg: 1420631834