

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Oxyn-Avenir 5/2.5 mg, Oxyn-Avenir 10/5 mg, Oxyn-Avenir 20/10 mg, Oxyn-Avenir 30/15 mg, Oxyn-Avenir 40/20 mg
Prolonged release tablets

Active ingredients:

Product	oxycodone hydrochloride	naloxone hydrochloride
Oxyn-Avenir 5/2.5 mg	5 mg	2.5 mg
Oxyn-Avenir 10/5 mg	10 mg	5 mg
Oxyn-Avenir 20/10 mg	20 mg	10 mg
Oxyn-Avenir 30/15 mg	30 mg	15 mg
Oxyn-Avenir 40/20 mg	40 mg	20 mg

For a list of the other ingredients see section 6.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

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

Medicines of the opioid group can cause addiction, especially with prolonged use, and have potential for abuse and overdose. The reaction to overdose can be slow breathing and even death. Make sure you know the name of your medicine, the dosage you are taking, how often you take it, the duration of your treatment, its side effects and potential risks. Additional information about the risk of dependence and addiction can be found at: https://www.health.gov.il/UnitsOffice/HD/MTI/Drugs/risk/DocLib/opioids_en.pdf

Taking this medicine with medicines in the benzodiazepine group, other medicines that depress the central nervous system (including psychoactive drugs) or alcohol may cause profound drowsiness, breathing difficulties (respiratory depression), coma and death.

1. What is this medicine intended for?

This medicine is intended for relieving moderate to severe pain.

Therapeutic group: oxycodone - opioid analgesic, naloxone - opioid antagonist.

There are two active ingredients in Oxyn-Avenir. The opioid ingredient of Oxyn-Avenir (oxycodone) is intended to relieve moderate or severe pain in patients who need constant round-the-clock pain relief for several days or more. The naloxone ingredient which is an opioid antagonist is added to reduce the constipation caused by the activity of the opioid oxycodone in the digestive system.

2. Before using this medicine:

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredients or to any of the other ingredients that these tablets contain (for a list of the other ingredients, see section 6)
- you have breathing problems, such as breathing more slowly or weakly than usual (severe respiratory depression), severe lung disease associated with narrowing of the airways (COPD), severe bronchial asthma
- you have cor pulmonale (in this condition, the right side of the heart becomes enlarged due to increased pressure in blood vessels in the lung, for instance)
- you have a bowel obstruction not caused by using opioids
- you have moderately to severely impaired liver function.

Special warnings about using this medicine:

Tell your doctor before starting treatment with Oxyn-Avenir if:

- you are an elderly or debilitated (weak) patient
- you have a bowel obstruction caused by using opioids; impaired kidney function; mild liver function impairment; you have severely impaired lung function, pauses in breathing during sleep (may make you sleepy during the day); sleepiness; impaired thyroid function (myxedema or underactivity); gallstones; low or high blood pressure; heart disease (cardiovascular disease), enlarged prostate gland
- your adrenal gland is underactive (adrenal insufficiency, Addison's disease)
- you have a mental problem that is due to the toxic effect of medicines, alcohol or psychoactive drugs (toxic psychosis)
- you have a head injury (due to the risk of increased pressure in the brain); inflamed pancreas; epilepsy or seizures (or you tend to have convulsions)
- you have ever had an addiction to alcohol, medicines, or psychoactive drugs, or withdrawal symptoms when stopping them, such as agitation, anxiety, tremor or sweating
- you have cancer associated with peritoneal metastases or the beginning of a bowel obstruction due to advanced stages of digestive or pelvic cancer.

Also tell your doctor if you have had the abovementioned conditions in the past, and/or if they develop while you are taking this medicine.

- The most serious result of opioid overdose is respiratory depression (slow and shallow breathing), which could also cause a reduction in blood oxygen, resulting in effects such as fainting.
- Chewing or crushing the tablets may impair the prolonged release mechanism of oxycodone in the tablet and lead to the absorption of a potentially life-threatening dose of oxycodone (see under 'If you have accidentally taken a higher dosage').
- If you experience severe diarrhea at the start of treatment (during the first 3-5 days), this may be due to the effect of naloxone. If diarrhea persists for longer than 3 to 5 days or gives you cause for concern, consult your doctor.
- If before starting treatment with Oxyn-Avenir you were using another opioid, withdrawal symptoms (such as restlessness, sweating, muscle pain) are possible when you start treatment with Oxyn-Avenir. If you experience withdrawal symptoms, you may need to be monitored more closely by your doctor.
- Prolonged use may cause tolerance (need for a higher dose to achieve the desired effect), as well as addiction. Withdrawal symptoms may occur if treatment is stopped suddenly. When you no longer need treatment, you should reduce your daily dose gradually, in consultation with your doctor.
- As with other opioid pain relievers, there is a risk of developing (psychological) dependence on this medicine. Avoid oxycodone treatment if you have ever had an addiction to alcohol, psychoactive drugs, or medicines.
- If you are about to have surgery, tell the doctor that you are taking this medicine.
- **Misuse of Oxyn-Avenir:** Oxyn-Avenir is not intended or suitable for treating withdrawal symptoms.

Do not abuse these tablets; taking the tablets not by mouth or taking them not according to your doctor's instructions may cause life-threatening side effects or withdrawal effects.

- Use of this medicine may cause a positive result in anti-doping tests.

Use in children and adolescents: There is no information about the safety and efficacy of using this medicine in children and adolescents under 18 years old so its use is not recommended.

Tests and follow-up: During long-term treatment, you must undergo periodic evaluations to assess your ongoing need for the medicine.

Other medicines and Oxyn-Avenir: If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

- other strong pain relievers (opioids); sleep and tranquilizing medicines including benzodiazepines; antidepressants; medicines used to treat allergies, nausea/vomiting, or travel sickness (antihistamines or antiemetics); medicines for treating mental disorders such as phenothiazines, antipsychotics or neuroleptics
- anticoagulants (such as coumarin derivatives); antibiotics of the macrolide group (such as clarithromycin, erythromycin, telithromycin); antifungal medicines of the azole group (such as ketoconazole)
- protease inhibitors (used to treat HIV) such as ritonavir; cimetidine (used to treat heartburn, gastric ulcer, indigestion); rifampicin (used to treat tuberculosis); carbamazepine (used to treat seizures and certain pain conditions), phenytoin (used to treat seizures)
- the *Hypericum* plant (also called St. John's wort); quinidine (used to treat heart rhythm disorders)
- monoamine oxidase inhibitors (such as linezolid) also used to treat depression or Parkinson's disease
- medicines with anticholinergic activity (such as medicines used to treat Parkinson's disease, medicines for relaxing the muscles).

Using this medicine and food: You can take the medicine regardless of mealtimes.

Avoid drinking grapefruit juice when using this medicine.

Using this medicine and alcohol consumption: Do not drink alcohol during the course of treatment with this medicine.

Drinking alcohol while you are taking this medicine may make you feel sleepier or increase the risk of serious side effects such as breathing difficulties (shallow breathing) with a risk of paused breathing, and loss of consciousness.

- **Pregnancy and breastfeeding:** If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice.
- Do not use this medicine if you are pregnant (unless otherwise instructed by your doctor). Prolonged use during pregnancy may cause withdrawal symptoms in the newborn. Use during childbirth may cause breathing problems in the newborn (respiratory depression).
- The active ingredient oxycodone passes into breast milk, so do not breastfeed during the course of treatment.

Driving and using machines: Using this medicine can impair your ability to drive as it may cause dizziness or sleepiness (especially when you start treatment, when the dosage is increased, when switching from another medicine, or when taken in combination with other medicines that affect the central nervous system). If you feel drowsy and/or any other effect that could influence your driving, do not drive, operate machines, or participate in activities that require alertness. Consult your doctor if necessary.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. **Only your doctor will determine your dose and how you should take this medicine.** Oxyn-Avenir tablets have a prolonged release mechanism. The active ingredients are released over 12 hours.

Chewing or crushing the tablets may impair the prolonged release mechanism of the tablet and lead to the absorption of a potentially life-threatening dose of oxycodone (see under 'If you have accidentally taken a higher dosage').

The tablets should be taken at set times (usually every 12 hours), as determined by your doctor. Your doctor will adjust your dose to your individual condition and intensity of pain. The doctor will prescribe the minimum dose needed to control your pain.

Do not exceed the recommended dose.

If your doctor switches you from Oxyn-Avenir to another opioid, your bowel function may get worse.

If you experience pain between doses, contact your doctor. You may need to get a fast-acting pain-reliever. Oxyn-Avenir is not suitable for this.

If you feel that the effect of the tablets is too strong or too weak, contact your doctor.

Elderly patients: If liver and kidney function are normal, no dose adjustment is usually necessary.

Patients with kidney function problems or mild liver function problems: Your doctor may prescribe a lower dose.

This medicine is not intended for patients with moderate to severe liver problems.

How to use: Take your tablets with half a glass of water every 12 hours, regardless of mealtimes. For example, at 8 in the morning and at 8 in the evening. Oxyn-Avenir 5/2.5 mg: Take the tablets whole; do not split, break, chew or crush the tablets.

Oxyn-Avenir 10/5; Oxyn-Avenir 20/10 mg; Oxyn-Avenir 30/15 mg; Oxyn-Avenir 40/20 mg: You may split the tablet into two equal parts. Do not break, chew, or crush the tablet.

Duration of use: Do not take the tablets for a longer period than necessary. If you are on long-term treatment, your doctor will perform follow-up tests to check whether you need to continue taking the treatment.

If you have accidentally taken a higher dosage or if a child or any other person has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you. Symptoms of overdose may include: constriction of the pupils in the eyes, respiratory depression (slower and weaker breathing than normal), drowsiness up to losing consciousness, decrease in muscle tone, decrease in pulse, drop in blood pressure. In severe cases, coma, fluid on the lungs, and circulatory collapse (shock) may occur. These symptoms can be life threatening and require urgent medical attention. Do not drive or perform activities that require alertness if you have taken an overdose.

If you forget to take the medicine, follow the instructions below: If there are 8 or more hours until the next dose is due: take the forgotten dose immediately. Take the next dose at the usual time. If there are less than 8 hours until the next dose is due: Take the forgotten dose and then wait 8 hours before taking your next dose.

Afterwards, try to get back on track with your regular dosing schedule. Consult your doctor if you are not sure.

Make sure to have an interval of at least 8 hours between doses. Do not take a double dose to make up for a forgotten dose.

Adhere to the treatment as recommended by your doctor. Even if your health improves, do not stop taking this medicine without consulting your doctor.

If you stop taking this medicine: If you do not need treatment any more, consult your doctor who will guide you how to gradually reduce your daily dosage in order to reduce the risk of withdrawal symptoms such as: restlessness, excessive sweating, muscle pain.

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

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using Oxyn-Avenir may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Contact your doctor immediately if you experience the following side effects:

- respiratory depression, the most serious side effect of this medicine, in which breathing becomes slower and weaker. It mostly may occur in elderly and debilitated/weak patients.
- severe decrease in blood pressure.

Additional side effects:

Common side effects (affect 1-10 in 100 users): abdominal pain, constipation, diarrhea, dry mouth, indigestion, vomiting, nausea, flatulence, decreased appetite (up to loss of appetite), dizziness or spinning sensation, headache, hot flashes, general weakness, tiredness/exhaustion, skin reactions such as itching or rash, excessive sweating, vertigo, sleeping difficulties, drowsiness.

Uncommon side effects (affect 1-10 in 1,000 users): abdominal bloating, unusual thoughts, anxiety, confusion, depression, irritability, chest pain/tightness (especially if you already have coronary heart disease), reduced or increased blood pressure, withdrawal symptoms such as agitation, fainting, lack of energy, thirst, altered sense of taste, palpitations (throbbing heartbeat), gallbladder pain (colic), angina pectoris, feeling generally unwell, pain, swelling of hands, ankles, or feet; difficulty concentrating, difficulty speaking, shaking, shortness of breath or breathing difficulties, restlessness, chills, increased liver enzymes, reduced sexual drive, runny nose, cough, hypersensitivity or allergic reactions, weight loss, increased risk of injury from accidents, increased urge to urinate, muscle pain, muscle cramps or twitches, vision impairment, convulsions (especially in epileptic patients or patients with a seizure tendency).

Rare side effects (affect 1-10 in 10,000 users): increased pulse, dental (teeth) changes, weight gain, yawning, dependence on the medicine.

Side effects of unknown frequency (the frequency of these effects has not been established yet): feeling extreme happiness (euphoria), severe drowsiness (sedation), erection problems, nightmares, hallucinations, shallow breathing, difficulty passing urine (urinary retention), tingling, belching.

Other side effects observed during use of medicines that contain the active ingredient oxycodone alone:

constriction of pupils, reduced cough reflex.

Common side effects (affect 1-10 in 100 users): changes in behavior or mood, increased or reduced activity, hiccupping.

Uncommon side effects (affect 1-10 in 1,000 users): migraines, increased muscle tone, involuntary muscle contractions, dependence on the medicine, bowel obstruction, dry skin, tolerance to the medicine, reduced sensitivity to pain or touch, impaired coordination, changes in voice, fluid retention (edema), hearing impairment, ulcers/inflammation in the mouth, difficulties in swallowing, sore gums, perceiving reality incorrectly, skin redness, widening of blood vessels, dehydration, agitation, reduced levels of sex hormones (which may affect sperm production in men and menstrual cycle in women).

Rare side effects (affect 1-10 in 10,000 users): urticaria (itchy rash), infections such as herpes or cold sores (may appear as blisters around the mouth or genitals), increased appetite, black (bloody) stools, bleeding gums.

Side effects of unknown frequency (the frequency of these effects has not been established yet): severe generalized allergic reaction (anaphylactic reaction), increased sensitivity to pain, absence of menstrual periods in women, withdrawal symptoms in the newborn, aggression, problems with bile flow, dental caries.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

If you do not need these tablets any more, ask your pharmacist how to dispose of them.

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

Storage conditions: Store below 25°C.

6. Additional information

In addition to the active ingredients these tablets also contain:

Tablet core: polyvinyl acetate, microcrystalline cellulose, povidone, sodium lauryl sulphate, silica colloidal anhydrous, magnesium stearate.

Tablet coating:
Oxyn-Avenir 5/2.5 mg: polyvinyl alcohol, titanium dioxide, macrogol 3350, talc.
Oxyn-Avenir 10/5 mg: polyvinyl alcohol, titanium dioxide, iron oxide red (E172), macrogol 3350, talc.
Oxyn-Avenir 20/10 mg: polyvinyl alcohol, titanium dioxide, macrogol 3350, talc.
Oxyn-Avenir 30/15 mg: polyvinyl alcohol, titanium dioxide, iron oxide yellow, macrogol 3350, talc.
Oxyn-Avenir 40/20 mg: polyvinyl alcohol, titanium dioxide, iron oxide red, macrogol 3350, talc.

What the medicine looks like and contents of the pack:

Oxyn-Avenir 5/2.5 mg: white, round, biconvex film-coated tablet.
Oxyn-Avenir 10/5 mg: pink, oblong, biconvex film-coated tablet with a score line on both sides. You may split the tablet into two equal parts.
Oxyn-Avenir 20/10 mg: white, oblong, biconvex film-coated tablet with a score line on both sides. You may split the tablet into two equal parts.
Oxyn-Avenir 30/15 mg: yellow, oblong, biconvex film-coated tablet with a score line on both sides. You may split the tablet into two equal parts.
Oxyn-Avenir 40/20 mg: pink, oblong, biconvex film-coated tablet with a score line on both sides. You may split the tablet into two equal parts.

Each pack contains 20 tablets in blister cards. Not all pack sizes may be marketed.

Registration holder's name and address: BioAvenir Ltd., Israel, 1 David Hemelech St., Herzelia Pituach.

Manufacturer's name and address: Develco Pharma GmbH, Grienmatt 27 DE-79650, Schopfheim, Germany.

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

- Oxyn-Avenir 5/2.5 mg 165-60-35563-00
- Oxyn-Avenir 10/5 mg 165-61-35564-00
- Oxyn-Avenir 20/10 mg 165-62-35565-00
- Oxyn-Avenir 30/15 mg 165-63-35566-00
- Oxyn-Avenir 40/20 mg 165-64-35567-00

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