

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

The medicine is dispensed with a doctor's prescription only

**SUBOXONE film 2 mg/0.5 mg, for sublingual or buccal use**

**SUBOXONE film 4 mg/1 mg, for sublingual or buccal use**

**SUBOXONE film 8 mg/2 mg, for sublingual or buccal use**

**SUBOXONE film 12 mg/3 mg, for sublingual or buccal use**

**Active ingredients and their quantities in unit dose:**

SUBOXONE film 2 mg/0.5 mg, each film contains:

Buprenorphine (as hydrochloride) 2 mg

Naloxone (as hydrochloride dihydrate) 0.5 mg

SUBOXONE film 4 mg/1 mg, each film contains:

Buprenorphine (as hydrochloride) 4 mg

Naloxone (as hydrochloride dihydrate) 1 mg

SUBOXONE film 8 mg/2 mg, each film contains:

Buprenorphine (as hydrochloride) 8 mg

Naloxone (as hydrochloride dihydrate) 2 mg

SUBOXONE film 12 mg/3 mg, each film contains:

Buprenorphine (as hydrochloride) 12 mg

Naloxone (as hydrochloride dihydrate) 3 mg

Inactive ingredients - see section 6 "Further information".

**Read the 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 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.

**Important:**

SUBOXONE film should be kept in a safe place away from the reach of children.

Accidental use by a child is a medical emergency and can result in death. If a child accidentally uses SUBOXONE film, contact your doctor or emergency room immediately.

**1. What is the medicine intended for?**

SUBOXONE film is indicated for treatment of opioid dependence in adults and adolescents over 15 years of age. SUBOXONE sublingual film should be used as part of a complete treatment plan that includes counseling and psychosocial support.

**Therapeutic group:**

Buprenorphine- partial opioid agonist

Naloxone- opioid antagonist

## **2. Before using the medicine**

### **Do not use the medicine if:**

- you are sensitive (allergic) to the active ingredients (buprenorphine or naloxone) or to any of the other ingredients contained in the medicine (see section 6).
- you have severe liver problems.

### **Special warnings regarding use of the medicine**

#### **Before treatment with SUBOXONE film, tell your doctor if:**

- you suffer from liver or kidney dysfunction. Cases of hepatitis, increase in liver enzymes, liver failure, liver necrosis, renal liver syndrome, liver encephalopathy and even death have been reported.
- you suffer from breathing difficulties or lung problems [such as chronic obstructive pulmonary disease, pulmonary heart (cor pulmonale), oxygen deficiency (hypoxia) or previous respiratory depression].
- you suffer from an enlarged prostate gland (in men)
- you suffer from a head injury or brain problem
- you suffer from problems urinating
- you suffer from a curve in your spine that affects your breathing
- you suffer from gallbladder problems
- you suffer from adrenal gland problems
- you suffer from Addison's disease
- you suffer from under activity of the thyroid gland (hypothyroidism)
- you have a history of alcoholism
- you suffer from mental problems such as hallucinations (seeing or hearing things that do not exist)
- you suffer from blood pressure problems such as orthostatic hypotension
- you suffer from acute abdominal pain
- you suffer from some other medical problem
- Buprenorphine, the active ingredient in SUBOXONE film, can cause serious and life-threatening problems, especially if you take it or use it with certain other medicines or drugs. Call your doctor immediately or get emergency treatment if you:
  - o feel you are about to faint or are dizzy
  - o have mental changes such as confusion
  - o have slower breathing than you normally have
  - o are very sleepy
  - o have blurred vision
  - o have orientation problems
  - o have unclear speech
  - o cannot think well or clearly
  - o have slow reflexes
  - o have a high body temperature
  - o feel agitated
  - o have stiff muscles
  - o have trouble walking

These can be signs of an overdose or other serious problems.

- Do not substitute SUBOXONE film with other medicines containing buprenorphine without talking to your doctor. The amount of buprenorphine in a dose of SUBOXONE film is not the same as the amount of buprenorphine in other medicines containing buprenorphine. Your doctor will prescribe a starting dose of SUBOXONE film that may be different from the dose of other buprenorphine medicines that you may have taken.
- SUBOXONE film contains an opioid that can cause physical dependence.
  - o Do not stop taking SUBOXONE film without talking to your doctor. You may become

sick and suffer from uncomfortable withdrawal signs and symptoms because your body has become used to this medicine.

- o Physical dependence is not the same as drug addiction.
- o SUBOXONE film is not intended for occasional or “as needed” use.
  
- An overdose and even death can happen if you take benzodiazepines, tranquilizers, hypnotics or antidepressants while using SUBOXONE film. Ask your doctor what you should do if you take one of these medicines.
  
- Do not inject or snort SUBOXONE film.
- Snorting SUBOXONE film can cause withdrawal symptoms.
  
- Injecting SUBOXONE film may cause life-threatening infections and other serious health problems.
  
- Crushing and/or dissolving SUBOXONE film and then injecting it can cause serious withdrawal symptoms (sudden, serious withdrawal symptoms, such as pain, cramps, vomiting and diarrhea) in people with physical dependence on other opioids.
  
- In an emergency, make sure your family members tell the emergency room staff that you have a physical dependence on an opioid and that you are being treated with SUBOXONE film.
  
- Never give your SUBOXONE film to someone else; it can cause death or harm.
  
- SUBOXONE film contains buprenorphine, which can be a target for people who abuse prescription medicines or street drugs. Keep your SUBOXONE film in a safe place to protect it from theft, away from the sight and reach of children and in a place that is not accessible to others, including guests at home.

**Children and adolescents:**

SUBOXONE film is intended for use in adults and adolescents over 15 years of age. Due to limited information regarding adolescent use (ages 15-18), patients in this age group should be monitored closely. The safety and efficacy of use in children under 15 years of age have not been established.

**Tests and Follow-up:**

Before starting treatment and while taking SUBOXONE film your doctor will refer you for liver function tests.

**Drug interactions/reactions:**

**If you are taking, or have recently taken other medicines including over-the-counter medicines and nutritional supplements, tell your physician or pharmacist.** Especially if you take:

- **Other medicines that may make you feel sleepy**, such as muscle relaxants, analgesics (such as tramadol), antidepressants (such as mirtazapine, trazodone, phenelzine, linezolid), or antihistamines.
  
- Benzodiazepines or other central nervous system inhibitors (medicines for sedation, sleep, anxiety, muscle relaxation, general anesthesia, antipsychotics and other opioids). See section "Special warnings regarding use of the medicine".
  
- Macrolide antibiotics (such as erythromycin)
  
- Medicines to treat fungal infections (such as ketoconazole)
  
- Antiretroviral medicines (used to treat AIDS) such as: ritonavir, atazanavir, efavirenz,

nevirapine, etravirine, delaviradine

- Certain medicines may reduce the activity of SUBOXONE film. These include medicines to treat epilepsy (such as: carbamazepine or phenytoin) and a medicine to treat tuberculosis (rifampicin)
- Medicines to treat migraine (such as: triptans)
- Diuretics
- Anticholinergic drugs

SUBOXONE film may affect the way medicines work, and conversely, other medicines may affect the way SUBOXONE film works. Some medicines can cause serious or life-threatening medical problems when taken with SUBOXONE film. Sometimes, the dosage of certain medicines and SUBOXONE film should be changed if they are taken together. Do not take any medicine while using SUBOXONE film until you talk with your doctor. Your doctor will tell you if it is safe to take other medicines while taking SUBOXONE film.

### **Medicine use and alcohol consumption**

**Do not drink alcohol while using SUBOXONE film**, as this may result in loss of consciousness or even death.

### **Pregnancy, breastfeeding and fertility**

You should tell your doctor if you are pregnant or planning to become pregnant. If you are taking SUBOXONE film during pregnancy, your baby may have signs of opioid withdrawal at birth. Neonatal Opioid Withdrawal Syndrome (NOWS), is an expected and treatable outcome resulting from prolonged opioid use during pregnancy.

Tell your doctor if you are breastfeeding or plan to breastfeed. SUBOXONE film can pass into breast milk and may harm your baby. Talk to your doctor about the best way to feed your baby if you are taking SUBOXONE film. If you are taking SUBOXONE film while breastfeeding, you must keep track of signs of increased sleepiness and breathing problems in your baby.

Chronic use of opioids may cause reduced fertility in women and men. It is not known whether this effect of SUBOXONE on fertility is reversible or not.

### **Driving and using machines**

**Do not drive, operate heavy machinery or perform other dangerous activities until you know how this medicine affects you.** Buprenorphine can cause drowsiness and a slowed reaction time. This may happen more often in the first few weeks of treatment when your dose changes, but can also happen with drinking alcohol or taking other sedative drugs while taking SUBOXONE film.

## **3. HOW SHOULD YOU USE THE MEDICINE?**

- Always use the preparation according to the doctor's instructions.
- The dosage and the treatment regimen will be determined by the doctor only. During treatment, your doctor may adjust the dose depending on your response. Do not change the dose unless your doctor tells you to. You should check with your doctor or pharmacist if you are not sure about the dosage and treatment regimen of the preparation.
- **Do not exceed the recommended dose.**
- SUBOXONE film should be taken once a day.

- SUBOXONE film is intended for sublingual or buccal administration. At the beginning of treatment, SUBOXONE film should **only** be taken under the tongue (sublingual administration). After a few days, you can choose whether to take SUBOXONE film by placing it on the inside of the cheek (buccal administration) or by taking it sublingually.
- Your doctor will show you how to take SUBOXONE film the right way.
- Each SUBOXONE film comes in a sealed child-resistant foil pouch. Do not open the foil pouch until you are ready to use the medicine.

**Taking SUBOXONE film:**

- To open the SUBOXONE film foil pouch, fold along the dotted line (see Figure 1).

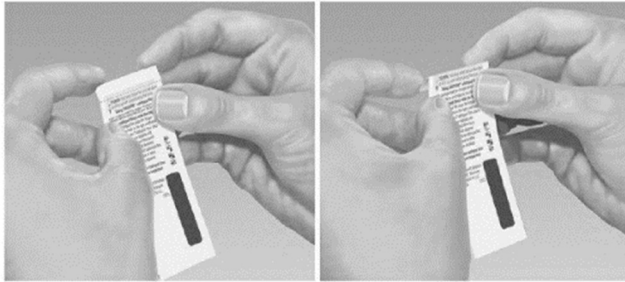


Figure 1

- Tear the pouch along the slit or cut with scissors along the arrow (see Figure 2).

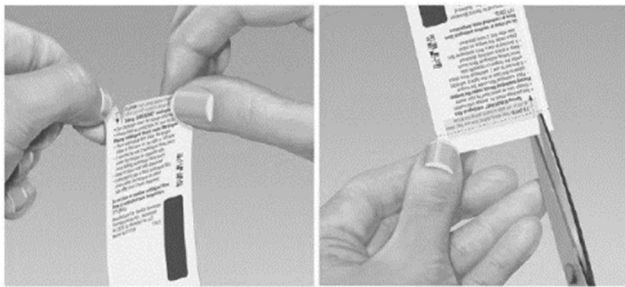


Figure 2

- Before taking SUBOXONE film, drink water to wet your mouth. This helps the film dissolve more easily.

**Taking SUBOXONE film under the tongue (sublingual administration):**

- Hold the film between two fingers by the outside edges.
- **Place the SUBOXONE film under the tongue**, close to the base of the tongue, on either to the left or right side of the center (see Figure 3).



Figure 3

- If your doctor tells you to take two films at the same time, place the second film under your tongue on the opposite side. Avoid contact between the films.
- Leave the films in place until completely dissolved.
- If your doctor tells you to take a third film, place it under your tongue on either side

after the first two films have dissolved.

**Taking SUBOXONE film on the inside of the cheek (buccal administration):**

- Hold the film between two fingers by the outside edges.
- Place one film on the inside of your right or left cheek (see Figure 4).

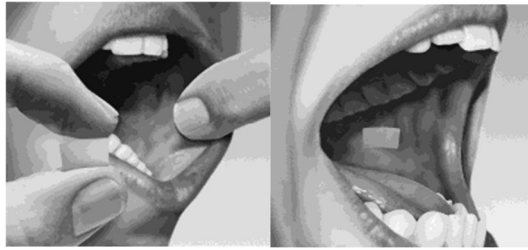


Figure 4

- If your doctor tells you to take two films at the same time, place the second film on the inside of the opposite cheek.
- Keep the films in place until completely dissolved.
- If your doctor tells you to take a third film, place it on the inside of your right or left cheek after the first two films have dissolved.

Suboxone film must be taken whole. **Do not cut, chew, crush or swallow** SUBOXONE film as the medicine will not work and you may get withdrawal symptoms. While SUBOXONE film dissolves, do not chew or swallow the film since the medicine will not work as well.

**Do not talk while taking the medicine.** Talking while the film dissolves can affect how well the medicine in SUBOXONE film is absorbed.

**If you accidentally take a higher dose,** the following side effects may appear: small pupils, feeling sleepy and uncoordinated (sedation), low blood pressure, respiratory depression and death. Immediately obtain urgent medical help.

If you have taken an overdose or if a child accidentally swallowed the medicine, immediately contact the doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

Cases of death have been reported after using an overdose of SUBOXONE film for pain relief. SUBOXONE film should not be used for analgesia.

**If you forgot to take this medicine** at the designated time, take your medicine when you remember. If the time for the next dose is very close, skip the missed dose and take the next dose at the regular time. Do not take a double dose, unless your doctor tells you to. If you are not sure about the dose, call your doctor.

Adhere to the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting your doctor.

**Do not stop taking SUBOXONE film suddenly.** You could become sick and suffer from withdrawal symptoms because your body has become used to the medicine. Physical dependence is not the same as drug addiction. Your doctor can tell you more about the differences between physical dependence and drug addiction. To reduce withdrawal symptoms, ask your doctor how to stop using SUBOXONE the right way.

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

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

#### **4. Side Effects**

As with any medicine, the use of SUBOXONE film 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.

**SUBOXONE film can cause serious side effects, including:**

- **See “Special warnings regarding use of the medicine”**
- **Respiratory problems.** You have a higher risk of death and coma if you take SUBOXONE film with other medicines, such as benzodiazepines.
- **Sleepiness, dizziness, and problems with coordination**
- **Dependency or abuse**
- **Liver problems.** Call your doctor right away if you notice any of the following signs of liver problems: yellowing of the skin or the white part of your eyes (jaundice), urine turning dark, stools turning light in color, you have less appetite, or you have stomach (abdominal) pain or nausea. See **“Special warnings regarding the use of the medicine/Tests and Follow up”**.
- **Allergic reaction.** You may have a rash, hives, swelling of the face, wheezing, or a decrease in blood pressure and loss of consciousness. Call a doctor or get emergency help right away.
- **Opioid withdrawal.** This can include: shaking, sweating more than normal, feeling hot or cold more than normal, runny nose, watery eyes, goose bumps, diarrhea, vomiting, and muscle aches. Tell your doctor if you develop any of these symptoms.
- **Decrease in blood pressure.** You may feel dizzy if you get up too fast from sitting or lying down.
- **Adrenal insufficiency.** Cases of adrenal insufficiency have been reported with opioid use, often after one month from the start of treatment. **Contact your doctor immediately** if you have a constellation of any of the non-specific symptoms that include nausea, vomiting, anorexia, fatigue, weakness, dizziness and low blood pressure.
- **Increase in brain and spinal fluid pressure**
- **Increase in biliary tract pressure**

**Very common side effects (effects that appear in more than one user out of 10):**

- Drug withdrawal syndrome
- Nausea
- Headache
- Sweating
- Constipation
- Difficulty falling or staying asleep (insomnia)
- Pain
- Abdominal pain

**Common side effects (effects that appear in 1-10 users out of 100):**

- Redness in the mouth
- Decreased sensitivity in the mouth (numb mouth)
- Weakness
- Chills
- Infection
- Back pain
- Vascular dilation
- Diarrhea

- Vomiting
- Watery discharge from nose or blocked nose (rhinitis)
- Abscess
- Fever
- Flu symptoms
- Accidental injury
- Dyspepsia
- Anxiety
- Depression
- Dizziness
- Nervousness
- Drowsiness
- Increased cough
- Sore throat (pharyngitis)
- Teary eyes
- Fainting

**Uncommon side effects (effects that appear in 1-10 users out of 1000):**

- Tongue pain or discomfort
- Feeling lightheaded or drunk
- Disturbance in attention
- Irregular heartbeat (palpitations)
- Blurred vision

**Very common side effects (effects that appear in more than one user out of 10) that occur at the beginning of treatment with SUBOXONE film:**

- Restlessness
- Anxiety
- Goose bumps
- Stomach discomfort
- Irritability
- Headache
- Watery discharge from nose
- Cold sweat
- Joint pain
- Teary eyes

**Other side effects reported after the start of marketing of SUBOXONE film:**

Most common side effects: peripheral edema, inflammation of the oral mucosa (stomatitis), inflammation of the tongue and blisters and ulcers in the mouth or tongue.

Additional side effects:

- Androgen deficiency: Chronic use of opioids may lead to decreased sex drive, impotence, amenorrhea, or infertility
- Local reactions: burning sensation in the mouth

**If a side effect occurs, if any of the side effects get worse, 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 due to drug treatment" found on the home page of the Ministry of Health website ([www.health.gov.il](http://www.health.gov.il)), that directs to the online form for reporting side effects, or by entering the link: [/https://sideeffects.health.gov.il](https://sideeffects.health.gov.il)

## **5. How to store the medicine?**

- Avoid poisoning! This medicine and any other medicine must be kept in a safe and closed place out of the reach and sight of other family members, children and/or infants, 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) which appears on the package.



The expiry date refers to the last day of that month.

- SUBOXONE film should be stored at room temperature, below 25°C.

## **6. Further Information**

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

Polyethylene oxide, hydroxypropyl methylcellulose, maltitol, acesulfame potassium, lime flavour, citric acid, sodium citrate, FD&C yellow #6, and white ink.

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

- SUBOXONE film 2 mg/0.5 mg - each pouch contains a light orange film embossed with "N2" in white
- SUBOXONE film 4 mg/1 mg - each pouch contains a light orange film embossed with "N4" in white
- SUBOXONE film 8 mg/2 mg - each pouch contains a light orange film embossed with "N8" in white
- SUBOXONE film 12 mg/3 mg - each pouch contains a light orange film embossed with "N12" in white

The package contains 30 pouches, and each pouch has one SUBOXONE film.

Registration holder and address: Naomi Shaco-Ezra Ltd, P.O. Box 6825, Ramat Gan.

Manufacturer and address: Aquestive Therapeutics, Indiana, USA for Indivior Inc, Virginia, USA.

This leaflet was determined and approved by the Ministry of Health in April 2020.

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

SUBOXONE film 2mg/0.5mg, 164-25-35832-00

SUBOXONE film 4 mg/1 mg, 164-26-35833-00

SUBOXONE film 8mg/2mg, 164-27-35834-00

SUBOXONE film 12mg 3mg, 164-28-35831-00