PACKAGE LEAFLET: INFORMATION FOR THE USER

Subutex 0.4mg, 2mg and 8mg sublingual tablets
buprenorphine

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Subutex is and what it is used for
2. Before you take Subutex
3. How to take Subutex
4. Possible side effects
5. How to store Subutex
6. Contents of the pack and further information

1. WHAT SUBUTEX IS AND WHAT IT IS USED FOR

Subutex is used to treat dependence on opiate (narcotic) drugs, such as morphine and heroin in opioid-dependent patients who have agreed to be treated for their opioid dependence. Subutex is used in adults and adolescents over 15 years of age who are also receiving medical, social and psychological support.

2. BEFORE YOU TAKE SUBUTEX

Do not take Subutex:

- If you are a child under the age of 15 years.
- If you are allergic (hypersensitive) to buprenorphine or to any of the other ingredients of this medicine (listed in section 6).
- If you have **serious breathing problems** or are having an acute asthma attack.
- If you have **serious problems with your liver**.
- If you are intoxicated due to alcohol or have trembling, sweating, anxiety confusion or hallucinations caused by alcohol.
- If you have recently had a head injury or have a condition that causes pressure to build up in your head.
- If you are breast feeding a baby.

Warnings and precautions
Talk to your doctor before taking Subutex if you have:

- asthma or other breathing problems
- any liver disease such as hepatitis
- low blood pressure
- an enlarged prostate gland or have difficulty when passing urine
- any kidney disease
- thyroid problems
- adrenocortical disorder (e.g. Addison’s disease)

- depression or other conditions that are treated with antidepressants. The use of these medicines together with Subutex can lead to serotonin syndrome, a potentially life-threatening condition (see `'Other medicines and Subutex").

Important things to be aware of:

•**Misuse, abuse and diversion**

This medicine can be a target for people who abuse prescription medicines, and should be kept in a safe place to protect it from theft. **Do not give this medicine to anyone else**. It can cause death or otherwise harm them.

•**Breathing problems**

Some people have died from respiratory failure (inability to breathe) because they misused this medicine or took it in combination with other central nervous system depressants, such as alcohol, benzodiazepines (tranquilisers), or other opioids.

•**Sleep-related breathing disorders**

Subutex can cause sleep-related breathing disorders such as sleep apnoea (breathing pauses during sleep) and sleep related hypoxemia (low oxygen level in the blood). The symptoms can include breathing pauses during sleep, night awakening due to shortness of breath, difficulties to maintain sleep or excessive drowsiness during the day. If you or another person observe these symptoms, contact your doctor. A dose reduction may be considered by your doctor.

•**Dependence**

This product can cause dependence.

•**Withdrawal symptoms**

This product can cause withdrawal symptoms if you take it less than 6 hours after you use a short-acting opioid (e.g. morphine, heroin) or less than 24 hours after you use a long-acting opioid such as methadone.

Subutex can also cause withdrawal symptoms if you stop taking it abruptly.

•**Liver damage**

Liver damage has been reported after taking Subutex, especially when the medicine is misused. This could also be due to viral infections (chronic C hepatitis), alcohol abuse, anorexia or use of other medicines with the ability to harm your liver (see section 4). **Regular blood tests may be conducted by your doctor to monitor the condition of your liver. Tell your doctor if you have any liver problems before you start treatment with Subutex.**

•**Blood pressure**

This product may cause your blood pressure to drop suddenly, causing you to feel dizzy if you get up too quickly from sitting or lying down.

•**Diagnosis of unrelated medical conditions**

This medicine may mask pain symptoms that could assist in the diagnosis of some diseases. Do not forget to advise your doctor if you take this medicine.

Other medicines and Subutex

Tell your doctor if you are taking, have recently taken or might take any other medicines.

Some medicines may increase the side effects of Subutex and may sometimes cause very serious reactions. Do not take any other medicines whilst taking Subutex without first talking to your doctor, especially:

- Concomitant use of Subutex and sedative medicines such as benzodiazepines or related drugs increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible.
  However if your doctor does prescribe Subutex together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor.
  Please tell your doctor about all sedative medicines you are taking and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

- anti-depressants such as moclobemide, tranylcypromine, citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, duloxetine, venlafaxine, amitriptyline, doxepine, or trimipramine. These medicines may interact with Subutex and you may experience symptoms such as involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, hallucinations, coma, excessive sweating, tremor, exaggeration of reflexes, increased muscle tension, body temperature above 38°C. Contact your doctor when experiencing such symptoms.

- **Other medicines that may make you feel sleepy** which are used to treat illnesses such as anxiety, sleeplessness, convulsions / seizures, pain. These types of medicines will reduce your alertness levels making it difficult for you to drive and use machines. They may also cause central nervous system depression, which is very serious. Below is a list of examples of these types of medicines:
  - other opioid containing medicines such as methadone, certain pain killers and cough suppressants.
  - antidepressants (used to treat depression) such as isocarboxazide and valproate may increase the effects of this medicine.
  - sedative H_1 receptor antagonists (used to treat allergic reactions) such as diphenhydramine and chlorphenamine.
  - barbiturates (used to cause sleep or sedation) such as phenobarbital, secobarbital
  - tranquilisers (used to cause sleep or sedation) such as chloral hydrate.

- Naltrexone may prevent Subutex from working. If you take naltrexone whilst you are taking Subutex you may experience a sudden onset of prolonged and intense withdrawal symptoms.
- Clonidine used to treat high blood pressure) may extend the effects of this medicine.
- Anti-retrovirals (used to treat AIDS) such as ritonavir, nelfinavir, indinavir may increase the effects of this medicine.
- Some antifungal agents (used to treat fungal infections) such as ketoconazole and itraconazole and certain antibiotics (macrolide) may extend the effects of this medicine.
- Some medicines may decrease the effect of Subutex. These include medicines used to treat epilepsy (such as carbamazepine and phenytoin) and medicines used to treat tuberculosis (rifampicin).

To get the greatest benefit from taking Subutex, you must tell your doctor about all the medicines you are taking, including alcohol, medicines containing alcohol, street drugs, and any prescription medicine you are taking that has not been prescribed for you by your doctor.

Taking Subutex with food and drink

Alcohol may increase drowsiness and may increase the risk of respiratory failure if taken with Subutex. **Do not take Subutex together with alcohol.** Do not swallow or consume food or drink until the tablet is completely dissolved.

Pregnancy and breast-feeding

Tell your doctor if you are pregnant or intend to become pregnant.

When taken during pregnancy, particularly late pregnancy, medicines like Subutex may cause drug withdrawal symptoms including problems with breathing in your newborn baby. These symptoms may occur several days after birth.

Do not breast feed your baby whilst taking this medicine as Subutex passes into breast milk.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Subutex may cause drowsiness. This may happen more often in the first few weeks of treatment when your dose is being changed, but can also happen if you drink alcohol or take sedative medicines when you take Subutex. Do not drive, use any tools or machines, or perform dangerous activities until you know how this medicine affects you.

Subutex contains lactose and sodium
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine. This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium free'.

3. HOW TO TAKE SUBUTEX

You must place the tablet under your tongue (sublingual) and allow it to dissolve, which will take 5 to 10 minutes. This is the only way to take the tablets. Do not chew or swallow them whole, as they will not work.

Your doctor will tell you how many tablets to take and you should always follow this advice.

To avoid sudden withdrawal symptoms, treatment with Subutex should be given when there are already clear signs of withdrawal symptoms.

Adults and children over the age of 15 years: when beginning treatment the dose is between 0.8 to 4mg, taken once a day.

For opioid-dependent patients who have not had any withdrawal treatment: one dose of Subutex should be taken at least 6 hours after the last use of the opioid (narcotic such as morphine or heroin), or when the first signs of craving appear. If you take it less than six hours after you use a narcotic you may get withdrawal symptoms.

For patients taking methadone: before beginning treatment, your doctor should reduce your dose of methadone to not more than 30mg a day. Subutex may cause withdrawal symptoms in patients who are dependent on methadone if you take it less than 24 hours after you use methadone.

During your treatment, your doctor may increase your dose of Subutex, to a maximum single daily dose of 32mg, depending upon your response. Once you have been stable for a while, your doctor will gradually reduce your dose and it may be possible to stop it altogether. Do not suddenly stop taking the tablets, as this may cause withdrawal symptoms.

If you take more Subutex than you should

If you or someone else takes too much of this medicine, you must go or be taken immediately to an emergency centre or hospital as overdose with Subutex may cause serious and life-threatening breathing problems.

If you forget to take Subutex

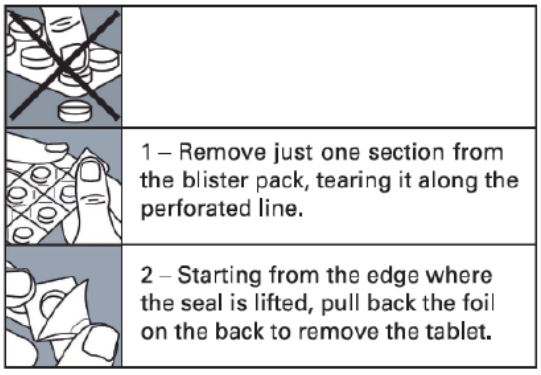
You should tell your doctor and follow his or her instructions. Do not take a double dose to make up for the forgotten dose.

If you stop taking Subutex

Do not change the treatment in any way or stop treatment without the agreement of the doctor who is treating you. Stopping treatment suddenly may cause withdrawal symptoms.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

How to remove the tablet from the blister pack



4. POSSIBLE SIDE EFFECTS

Like all medicines, Subutex can cause side effects, although not everybody gets them.

Tell your doctor immediately and seek urgent medical attention if you experience any of the following serious effects such as:

- sudden wheezing, difficulty breathing, swelling of the eyelids, face, tongue, lips, throat or hands; rash or itching especially those covering your whole body. These may be signs of a life-threatening allergic reaction.
- if you start to breath more slowly or weakly than expected (respiratory depression)
- if you start to feel faint, as this may be a sign of low blood pressure.
- severe fatigue (tiredness), have no appetite or if your skin or eyes look yellow. These may be symptoms of liver damage.

Side effects reported with Subutex

Very common side effects (may affect more than 1 in 10 people):
Drug withdrawal syndrome, headache, hyperhidrosis (sweating), insomnia (inability to sleep), nausea (feeling sick), pain
Common side effects (may affect up to 1 in 10 people):
Abdominal pain, agitation, anxiety, joint pain, asthenia, back pain, bone pain, bronchitis, chest pain, chills, constipation, cough, decreased appetite, depression, diarrhoea, dizziness, dry mouth, menstrual cramping/painful menstruation, upset stomach or other stomach discomfort, dyspnoea, wind, gastrointestinal disorder, hostility, hypertonia, infection, influenza, nervousness, increased tearing (watering eyes) or other tearing disorder, swollen glands (lymph nodes), feeling of general discomfort, faintness and dizziness, migraine, muscle spasms, muscle pain, large pupil size, neck pain, palpitations, paranoia, tingling, swollen arm or leg, sore throat and painful swallowing, fever, rash, change of colour, appearance or texture of the skin, somnolence, syncope (fainting), thinking abnormal, tooth disorder, tremor; enlargement of blood vessels, vomiting (being sick), yawning
Not known (frequency cannot be estimated from the available data):
Drug dependence, drug withdrawal syndrome neonatal, seeing or hearing things that are not there (hallucinations), drop in blood pressure on changing position from sitting or lying down to standing, whirling or spinning sensation, unable or inability to urinate, redness, pain or swelling at the point of application (e.g. injection site), liver injury with or without jaundice, abnormal liver functional test, inflammation of the inner layer of the heart

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects
If you get any side-effects, talk to your doctor or pharmacist. This includes any possible side-effects not listed in this leaflet. You can also report side-effects directly via: HPRA Pharmacovigilance Website: www.hpra.ie.

By reporting side affects you can help provide more information on the safety of this medicine.

5. HOW TO STORE SUBUTEX

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the carton and foil. The expiry date refers to the last day of that month.
Do not store above 30°C. Store in the original package.
Do not use this medicine if you notice damaged blister pockets.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Subutex contains

The active substance is buprenorphine (as buprenorphine hydrochloride).
Each sublingual tablet contains 0.4mg, 2mg or 8mg of buprenorphine.

The other ingredients are lactose monohydrate, mannitol (E421), maize starch, povidone K30, citric acid, magnesium stearate and sodium citrate.

What Subutex looks like and contents of the pack

Subutex 0.4mg sublingual tablets are uncoated oval white tablets of 8 mm x 4 mm, debossed with “04” on one side.

Subutex 2mg sublingual tablets are uncoated oval white tablets of 10 mm x 5 mm, debossed with “B2” on one side.

Subutex 8mg sublingual tablets are uncoated oval white tablets of 14 mm x 7 mm, debossed with “B8” on the one side.

The sublingual tablets come in nylon/aluminium/uPVC blister packs containing either 7 or 28 tablets.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer responsible for batch release

Indivior Europe Limited
27 Windsor Place
Dublin 2
D02 DK44
Ireland

For any information about this medicine, please contact the Marketing Authorisation Holder:

Ireland:
Indivior Europe Limited - **Telephone 1800554156**

Malta:
Indivior Europe Limited - **Telephone 80062185**

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This leaflet was last revised 05/2021.