Patient Leaflet According to the Pharmacists' Regulations (Preparations) – 1986

This medicine is sold with a doctor's prescription only

Butrans 5, Butrans 10, Butrans 15, Butrans 20

Matrix type transdermal patches

Active ingredient:
Each patch of Butrans 5 contains Buprenorphine 5 mg and releases 5 mcg/hr.
Each patch of Butrans 10 contains Buprenorphine 10 mg and releases 10 mcg/hr.
Each patch of Butrans 15 contains Buprenorphine 15 mg and releases 15 mcg/hr.
Each patch of Butrans 20 contains Buprenorphine 20 mg and releases 20 mcg/hr.

For the list of the additional ingredients, see section 6.

- **The patches contain a strong painkiller (opioid).**
- **Ensure that the old patch is removed before applying a new patch.**
- **Do not cut the patches.**
- **Do not expose the patches to a heat source (such as hot water bottles).**
- **Avoid hot baths and/or hot showers whilst wearing the patch.**
- **If you develop a fever inform your doctor immediately.**
- **Follow the dosage and manner of usage instructions carefully and change your patch on the same day and at the same time 7 days later.**
- **If your breathing becomes shallow and weak remove the patch and seek medical attention.**

Read the entire leaflet carefully before using the medicine.
This leaflet contains concise information about the medicine. Keep this leaflet in case you need to read it again. If you have any further questions, please refer to your doctor or pharmacist.
This medicine has been prescribed to treat your condition. Do not pass it on to others. It may harm them, even if you think their medical condition is similar to yours.

This medicine is intended for use in adults.

Medicines of the opioids group may cause addiction, especially with prolonged use, and they have a potential for misuse and overdose. A reaction to an overdose may be manifested by slow breathing and may even cause death.
Make sure you know the name of the medicine, the dosage that you take, how often you take it, the duration of treatment, potential side effects and risks.
Additional information regarding the risk of dependence and addiction can be found at the following link:
https://www.health.gov.il/UnitsOffice/HD/MTI/Drugs/risk/DocLib/opioids_en.pdf

Taking this medicine along with medicines from the benzodiazepines group, other medicines which depress the central nervous system (including drugs) or alcohol may cause a feeling of profound drowsiness, breathing difficulties (respiratory depression), coma and death.

1. What is the medicine intended for?

This medicine is intended for relief of chronic moderate to severe pain that does not respond to non-opioid painkillers.
Therapeutic Group: Opioid analgesics.
This medicine has been prescribed for you only and should not be given to anyone else. Opioids may cause addiction and you may experience withdrawal symptoms if you stop taking them suddenly.
Make sure that you received an explanation from the doctor on the duration of treatment with the medicine, when it is appropriate to stop taking it and how to do so safely.
Butrans patches act through the skin. After application, the active ingredient (buprenorphine) passes through the skin into the blood. The action of each patch lasts for seven days.

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient (buprenorphine), or to any of the other ingredients the medicine contains (listed in section 6); or you have previously experienced an allergic skin reaction to patches containing buprenorphine.
- You suffer from a condition that affects or might affect your breathing (for instance severe impairment of the respiratory system functioning or serious impairment of the respiratory center in the brain). The symptoms can include shortness of breath, coughing, or slower or weaker breathing than expected.
- You suffer from drug or opiod addiction (dependency), or are currently undergoing a drug or opiod withdrawal process. Do not use Butrans to treat symptoms related to drug or opiod withdrawal.
- You are taking medicines belonging to the monoamine oxidase inhibitor group (MAOIs), or if you took such a medicine within the last two weeks. See also 'Drug interactions' section.
- You suffer from myasthenia gravis (muscular weakness).
- You have suffered in the past from withdrawal symptoms (such as agitation, anxiety, shaking, sweating) as a result of stopping drinking alcohol.

Special warnings regarding the use of this medicine:
Before (and during) treatment with Butrans tell your doctor if:

- You suffer from depression or other conditions treated with antidepressants. The use of these medicines together with Butrans can lead to serotonin syndrome, a potentially life-threatening condition (see "Drug interactions" section).
- You suffer or have suffered in the past from opioid, alcohol, medicine or drug addiction. See also "Do not use the medicine if" section.
- You have suffered in the past from withdrawal symptoms such as: agitation, anxiety, shaking, or sweating when you stopped usage of alcohol or drugs. See also "Do not use the medicine if" section.
- You feel you need to use more Butrans patches to get the same measure of pain relief. This phenomenon may be a sign that you are developing tolerance to the medicine or are becoming addicted to it. In such a case contact your doctor to consider whether it is necessary to change the dosage or replace the medicine with another painkiller.
- You are under the influence of alcohol.
- You suffer or have suffered in the past from seizures or convulsions. These may be more frequent while you are using this medicine.
- You are suffering from a brain injury or tumor, a head injury, or increased pressure in your skull whose symptoms may include severe headache or nausea. This is because Butrans may make these symptoms worse, or hide the extent of the head injury.
- You suffer from a reduction in level of consciousness or symptoms of shock that may include: pale, cold and clammy skin, dizziness or light-headedness, fast, shallow breathing, or sweating.
- You suffer from dizzy or fainting spells.
- You have severe liver problems.
- You recently underwent surgery.
- You have a fever, since this condition may lead to larger quantities of the active ingredient being absorbed. If you develop a fever tell your doctor immediately.
- You suffer from a severe impairment of the lung function. The symptoms may include shortness of breath and coughing. See also 'Do not use the medicine if' section.
- You suffer from a condition in which your breathing stops for a short time when you are sleeping, a condition called sleep apnea.

- You suffer from constipation.
- You suffer or have suffered in the past from mental problems.

Additional warnings:

- Butrans patches contain buprenorphine, an opioid substance, and have a potential for drug abuse. Do not give Butrans to another person. Take precautions in order to prevent the medicine from reaching other hands.
- Use of this medicine regularly, particularly for a long period, may cause addiction. Make sure you received an explanation from the doctor regarding the duration of treatment with the medicine, when it is appropriate to stop using it and how to do so safely.
- Addiction may cause withdrawal symptoms when you stop using the medicine. Withdrawal symptoms may include restlessness, sleeping difficulties, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increase in blood pressure, nausea, vomiting, diarrhea, loss of appetite, shaking, shivering, sweating. Before discontinuing the medicine, consult with your doctor who will guide you how to gradually reduce the dosage. It is important to not stop using the medicine suddenly since it will increase the risk that you will experience withdrawal symptoms. See also in section 3 “If you stop using the medicine”.
- Taking high or frequent doses of opioids increases the risk of addiction. Excessive use and abuse may lead to an overdose and even to death.
- In rare cases, increasing the medicine dosage may cause you to be more sensitive to pain. In this case, contact the doctor for consultation on the treatment.
- Breathing disturbances related to sleep: the medicine may cause breathing disturbances related to sleep such as sleep apnea (pauses in breathing while asleep) and hypoxemia (low oxygen levels in the blood) related to sleep. The symptoms may include: pauses in breathing while asleep, night awakening due to shortness of breath, difficult remaining asleep, excessive drowsiness during the day. If you or someone else in your surroundings observes these symptoms in you, contact your doctor. The doctor may recommend reducing the dosage.
- When using Butrans patches you may experience mild to moderate skin reactions at the site where you have applied the patch (including contact dermatitis). These reactions include redness, swelling, itching, rash, small blisters, pain or a burning sensation at the application site. Sometimes these reactions may be severe. In some cases the reaction may only begin after several months of treatment.
  Applying the patch according to the instructions for use in section 3 reduces the risk of experiencing these reactions.
  If you experience these symptoms, remove the patch immediately and refer to your doctor. Continued use of the patches after experiencing an allergic reaction can result in blistering of the skin, open wounds, bleeding, ulceration, infections, changes to the color of the skin (hypo/hyperpigmentation), and dry, thick, scaly, scar-like patches.
- The medicine is not intended for acute pain relief.
- Periodically check (by sight or touch) the site where the patch has been applied, to verify that it is attached properly, is not loose and has not fallen off. If the patch is not attached properly, attach to the skin using an adhesive bandage (around it). Do not try and remove the patch and apply it to another site!

Children and adolescents:

This medicine is not intended for children and adolescents under 18 years of age.

Tests and follow-up:

- It is recommended to make an appointment for follow-up with the doctor a week or two weeks after starting the treatment in order to ensure that the dosage prescribed is optimal for you and to check whether you are suffering from any side effects of the medicine.
- In patients with liver diseases, your doctor may carry out closer monitoring.
- During long-term treatment, you need to undergo periodic assessments in order to evaluate the continued need for the medicine.

Drug interactions

If you are taking or have recently taken any other medicines, including non-prescription medicines and nutritional supplements, please tell your doctor or pharmacist. Certain medicines may increase the side effects of Butrans and may sometimes cause very serious reactions.

Especially inform your doctor or pharmacist if you are taking the following medicines (it should be noted that the following list indicates the active ingredients in the medicines. If you are not sure whether you are using one of these medicines, please consult with your doctor or pharmacist):
Using Butrans concomitantly with other medicines that depress the central nervous system can cause slow breathing or difficulty breathing (respiratory depression), severe sleepiness, loss of consciousness and death. For this reason the doctor will consider use of Butrans concomitantly with these medicines, when there are no other treatment options and only a low dosage and for short periods. These medicines include: Other opioid medicines for pain relief (such as morphine or codeine); antidepressants; anti-allergy medicines (antihistamines); sleep inducing medicines (such as benzodiazepines); anti-anxiety medicines; medicines to treat psychiatric/mental problems (such as phenothiazines); anesthetics (such as halothane); medicines to treat high blood pressure (such as clonidine); medicines from the monoamine oxidase inhibitors group (MAOIs) used for instance for treatment of depression, such as tranylcypromine, phenelzine, isocarboxazid, moclobemide, linezolid. Do not use Butrans if you are currently taking medicines from the MAOIs group or have taken them within the last two weeks.

If you or your surroundings (friends, family, caregivers) notice that you are having difficulty breathing or have become very sleepy or are losing consciousness refer to your doctor immediately.

Antidepressants such as citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, duloxetine, venlafaxine, amitriptyline, doxepin or trimipramine, or other serotonergic medicines: These medicines may cause a drug interaction with Butrans (serotonin syndrome which may be life-threatening). The symptoms may include: involuntary, rhythmic contractions of muscles, including the muscles that control eye movement; changes in the mental condition (such as agitation, hallucinations), coma, excessive sweating, shaking, exaggeration of reflexes, increased muscle tension, digestive system symptoms, body temperature above 38 °C. Contact the doctor if you experience these symptoms.

Medicines that might reduce the effect of Butrans such as: carbamazepine, phenobarbital, phenytoin (used to treat seizures inter alia), rifampicin (for treatment of tuberculosis).

Use of the medicine and alcohol consumption:

Do not drink alcohol during the treatment period with this medicine. Alcohol may make some of the side effects worse and may make you may feel unwell. In addition, drinking alcohol while using Butrans may affect your reaction time.

Pregnancy and breastfeeding:

- **Pregnancy**: Do not use Butrans if you are pregnant, think you are pregnant or are planning a pregnancy. If the medicine is used during pregnancy the newborn may suffer from respiratory depression and also may develop dependence on the medicine and experience withdrawal symptoms after the birth, which may need to be treated. The symptoms may include: restlessness, hyperactivity, abnormal sleeping patterns, high-pitched crying, tremor, vomiting, diarrhea, lack of weight gain.
- **Childbirth**: Use during childbirth may cause respiratory depression in the newborn that will need appropriate treatment after the birth.

- **Breastfeeding**: Do not use the medicine during the breastfeeding period, since the active ingredient (buprenorphine) passes into breastmilk and can affect the baby (may cause

respiratory depression in the baby).

- Likewise, do not use Butrans in women who may become pregnant and are not using contraceptives.

Driving and use of machinery:

- The use of this medicine may impair alertness and ability to react (e.g. in cases of unexpected or sudden occurrences). This phenomenon may occur especially: at the beginning of treatment, when the dosage is increased, in combination with alcohol, in combination with specific medicines used to treat anxiety or for sleep.
- Do not drive while using the medicine until you know how it affects you.
- If you feel a phenomenon such as dizziness, drowsiness, blurred vision, do not drive or operate machinery while using Butrans, and for 24 hours after removing the patch.
- In any case, employ caution in driving a vehicle, operating dangerous machinery and in any activity requiring alertness (also for approximately 24 hours after removing the patch).

Talk to your doctor or a pharmacist if you are not sure whether it is safe for you to drive while using this medicine.

3. How to use this medicine?

Always use according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and manner of treatment with the medicine.
There are four different strengths of Butrans patches: 5, 10, 15 and 20.
The dosage and manner of treatment will be determined by the doctor only. Make sure that your prescribing doctor discussed with you the duration of the treatment with the medicine, the plan for discontinuing the treatment and how to gradually stop taking the medicine.

The standard dosage is usually:
One patch is generally intended for seven consecutive days of treatment, . and you should change to a new patch every seven days (once weekly on the same day of the week) preferably always at the same time. Since after 3 days the maximum effect of the dose is obtained, your doctor may change the dose of the patch, if necessary, after 3 to 7 days, until the correct dosage for pain relief is achieved**. In any case, do not use more than two patches simultaneously and up to a maximum total dose of 40 micrograms per hour.**
Do not exceed the recommended dose.
Use this medicine at set times as determined by your doctor.

During the treatment, your doctor may instruct you to use a higher or lower dosage, or to combine up to two patches. Do not cut or divide the patch.
If your doctor advised you to take other painkillers in addition to Butrans, strictly follow the doctor's instructions, otherwise you will not fully benefit from the treatment with Butrans.
If you feel that the effect of the medicine is too weak or too strong, consult your doctor.

Attention:
This medicine is intended for external use only.

Manner of use:
If you cannot apply the patch yourself, ask for assistance.
a. Before applying the patch

- Choosing where to apply the patch: choose a dry, clean site that is not irritated or red and not injured, without large scars and without hair (or nearly hairless), on the upper body (chest or back) or on the outer, upper part of the arms (see fig. 1).
- If necessary, the hair can be cut with scissors (do not shave), at the intended application site. Avoid applying in an area where the skin might fold.
- If the site intended for application needs to be cleaned, use cold or lukewarm water only (not hot). Do not use soap, alcohol, oils, lotions, creams, ointments or means that rub the skin, at the site intended for application of the patch. These substances might prevent the patch from sticking properly.
- After a hot shower or bath or on hot and humid days - it is important to ensure that the skin is completely dry and has cooled to normal temperature, before applying the patch.

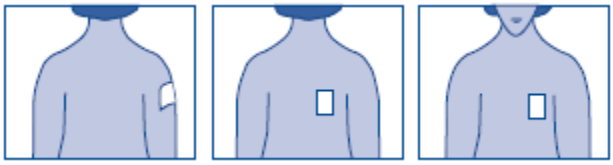

Fig. 1

b. Applying the patch

- Each patch is in in a sealed sachet. Just before use, open the sachet. Be careful not to damage the patch when opening the sachet. Remove the patch from the sachet. Do not use the patch if the sachet was not hermetically closed. Apply the patch immediately upon removing it from the sachet.
- Carefully remove one part of the protective aluminum foil covering the sticky side. Try not to touch the sticky side of the patch.
- Attach the patch to the skin at the chosen site and remove the second part of the aluminum foil, without touching the sticky side. Press the patch for 30 seconds with the palm of your hand to make sure that the contact is complete, especially at the edges (see fig. 2).
- Write down the date and time you applied the patch.

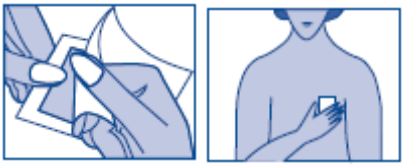

Fig. 2

c. While the patch is affixed to the skin

- Usually the patch should be left on the skin for seven consecutive days (a week). At the start of the treatment or when the intensity of the pain changes, the doctor may change the dosage already after the third day of application, until the correct dosage for pain relief is obtained. Write down the time of application (date/day and time).
- If the patch was applied correctly, the chance of it falling off is low. If the patch starts to peel off from the skin, you can tape it down with an adhesive bandage or suitable skin tape (around the edges). Do not try to remove the patch and apply to another site!
- Wait at least one hour after applying the patch before physical activity that causes sweating or before wetting the application site.
- You may bathe or swim while the patch is attached to the skin.
- While using the patch, avoid exposure of the application site to an external heat source such as a heating pad, hot water bottle, electric sheet or blanket, lamps (e.g. heating lamps), sauna, hot baths/showers, jacuzzi and so forth, in order to prevent increased absorption of the active ingredient from the patch and/or damage to the adhesiveness. In case of an increase in body temperature, the action of Butrans might change. Consult your doctor. See also “Special warnings regarding this use of the medicine” in section 2.

- In case the patch falls off, do not use it again, and apply another one instead. Apply the new patch to a different place on the skin. Write down the time of the new application (date and time). Inform your doctor that the patch fell off. The new patch should be replaced after seven days or according to your doctor's instructions.

d. Changing the patch

- Remove the used patch and fold it in half with the sticky side inwards.
- Open a sachet containing a new patch and take the patch out. Put the used patch inside the empty sachet. Dispose of the used patch in a hidden and safe place and out of the reach of children.
- Even used patches contain a certain amount of active ingredient that may harm children or animals. So make sure used patches are kept out of their reach and sight.
- Stick the new patch on a different appropriate place on the body. You can apply the patch to the same area again only after 3 to 4 weeks.
- It is recommended to change the patch at the same time of day.

e. Duration of treatment

- The doctor will decide for what time period you will be treated with the patches. Do not stop treatment without consulting your doctor. See the "If you stop taking the medicine" section.
- Do not keep at home patches that remain after completion of treatment with Butrans. If there are remaining patches that you do not need, consult your pharmacist.

If you have accidentally used a higher dosage: if you discovered that you accidentally used more patches than recommended by the doctor or if the patch accidentally stuck to a child or to someone who is not the patient, remove the patches immediately, proceed immediately to a doctor or hospital emergency room and bring the package of the medicine with you. Overdose symptoms might include: feeling very sleepy, nausea and vomiting. Breathing difficulties and loss of consciousness may also appear. Overdose symptoms require emergency medical attention. Recommended to request from the people around you to also be familiar with these symptoms and notice if they appear by you.

If you forget to apply a patch or if you forgot to change it:

If you forgot to apply the patch at the set time apply a new patch as soon as you remember, and write down the new time of the change (date and time). If you are very late with changing your patch, your pain may return. In this case, consult your doctor.

Under no circumstances is an additional patch to be applied, beyond what the doctor prescribed, to make up for the forgotten application.

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

If you stop using the medicine:

- Do not stop using the medicine suddenly. If you want to stop using the medicine, first consult the doctor who will guide you how to do this. The doctor will usually recommend that you gradually reduce the dosage in order to decrease the risk of the appearance of withdrawal symptoms such as: restlessness, sleeping difficulties, irritability, agitation, anxiety, feeling your heartbeat (palpitations), increase of blood pressure, nausea, vomiting, diarrhea, increased heart rate and/or breathing rate, loss of appetite, shaking, shivering, sweating, excessive secretions (tearing, runny nose), yawning, muscle pains, dilated pupils, abdominal cramps, weakness, excessive motility (also of the muscles).
- If you stop using Butrans too soon, your pain may return.

- The pain relieving effect of Butrans is maintained for some time after removal of the patch and so you should not start using another opioid medicine for 24 hours after removal of the patch.

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

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

4. Side effects

As with any medicine, use of Butrans 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.

Side effects that require special attention:

- **Allergic reaction:** The medicine can cause allergic reactions although a serious allergic reaction (for instance anaphylactic reaction) is rare. **Remove the patch and seek medical attention immediately if the following symptoms appear** that may indicate a serious allergic reaction: sudden wheezing, breathing difficulties, swelling of the eyelids, face or lips, rash and/or itching that can be over your whole body.
- **Allergic skin reactions**: You may experience allergic skin reactions at the application site. The symptoms can include rash, redness, itching, blisters, pain or a burning sensation, inflammation or swelling of the skin. In some cases these reactions may be severe. If you experience these symptoms, **remove the patch and refer to your doctor.** See also "Additional Warnings" in section 2.

- **Respiratory depression**: The most serious side effect is a condition where you breathe more slowly or weakly than usual and this can lead to severe sleepiness and loss of consciousness. This side effect may affect up to 1 out of 1,000 people and is more likely to occur when taken concomitantly with certain other medicines (see also "Drug interactions" in section 2). **Remove the patch and contact your doctor immediately, if this side effect appears.** Recommended to ask your surroundings (friends, family, caregivers) to pay attention if you develop these signs and symptoms.

- **Withdrawal symptoms:** When you stop taking the medicine, you may experience withdrawal symptoms. See "If you stop using the medicine" in section 3.

- **Addiction:** How to identify a state of addiction?
  Symptoms of addiction can include: a feeling that you need to use the patches for a longer period than recommended by the doctor and/or take a higher dose than that recommended by the doctor; use of the medicine for reasons other than those for which it was prescribed for you; when you stop using the medicine you feel unwell, and you feel well once more when you use the medicine again. If you feel these symptoms refer to your doctor.

Additional side effects (including frequencies):
Very common side effects (appear in more than 1 user out of 10):

- Headache, dizziness, drowsiness
- Constipation, nausea, vomiting
- Itchy skin, redness
- Skin reactions at the application site: rash, redness, itchiness, blisters, pain or burning sensation, inflammation or swelling/edema. In some cases these reactions can start after using the patches for some time. See also "Additional Warnings" in section 2.

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

- Loss of appetite.
- Confusion, depression, anxiety, difficulty in sleeping, irritability, shaking.
- Shortness of breath.
- Abdominal pain or discomfort, diarrhea, indigestion, dry mouth.
- Sweating, rash.
- Tiredness, unusual weakness, muscle weakness, swelling/edema of limbs (peripheral edema).

Uncommon side effects (appear in 1-10 users out of 1,000):

- Allergic reactions (hypersensitivity) including swelling of the face, lips or tongue, rash or itchiness.
- Loss of control of your mood, sleep disorders such as changes to your sleeping habits, restlessness, agitation, a feeling of extreme happiness (euphoria), hallucinations, reduced sexual drive, nightmares, aggressiveness, sedation.
- Feeling extremely drowsy, changes in taste, speaking impairment/difficulties, reduced sensitivity to pain or touch, numbness or tingling.
- Memory loss or impaired memory, migraines, fainting, problems with concentration or coordination.
- Dry eyes, blurred vision.
- A ringing or buzzing sound in the ears, vertigo (a feeling of dizziness or spinning).
- High or low blood pressure, chest pain, palpitations (feeling your heartbeat), fast or irregular heartbeat, flushing of the skin.
- Cough, hiccups, wheezing.
- Wind.
- Weight loss.
- Dry skin, urticaria (a raised, itchy rash)
- Muscle spasms, muscle pains.
- Urination impairments such as: loss of bladder control, incontinence, difficulty in beginning the flow of urine, inability to fully empty the bladder, urinary retention.
- Extreme fatigue, fever, chills (sudden feeling of cold with a high temperature and sweating), water retention (edema).
- An increase in accidental injuries (e.g. falls).
- Withdrawal symptoms when you stop the medicine, such as agitation, anxiousness, sweating, shaking (See also ”If you stop using the medicine” in section 3).
- Impaired liver functions (seen in blood tests, e.g.: increase in liver enzymes).

Rare side effects (appear in 1-10 users out of 10,000):

- A severe allergic reaction (anaphylactic reaction), the symptoms of which include difficulty breathing, wheezing, severe swelling of the face, lips or tongue, rash or itching, and loss of consciousness. See above “Side effects that require special attention”.
- Angina pectoris (chest pain associated with heart disease).
- Severe mental disorders causing loss of touch with reality (psychotic disorder).
- Impaired balance.
- Impairments/changes in your vision, swelling or puffiness/edema of the eyelids or face, a reduction in size of the pupils in the eye.
- Breathing difficulties, worsening of asthma, very fast breathing (hyperventilation).
- Dilated blood vessels, feeling of faintness, especially on standing up.
- Swallowing difficulties, intestinal obstruction.
- Swelling and irritation inside the nose (inflammation of the nose).
- Sexual dysfunction such as erection problems.
- Flu-like illness.
- Dehydration.

Very rare side effects (appear in less than 1 user out of 10,000);

- Mood swings.
- Involuntary muscle twitching.
- Ear pain.
- Blisters/pustule (abscesses).

Side effects of unknown frequency (effects whose frequency has not yet been determined):

- Spasms or seizures.
- Inflammation of the bowel wall (its symptoms may include fever, vomiting, stomach pain or discomfort).
- Colicky abdominal discomfort and pain that can derive from biliary colic.
- Feeling detached from oneself.
- Increased sensitivity to pain.
- Development of a condition where your breathing stops for a short period while you are asleep (sleep apnea).
- A need to use more patches to obtain the same level of pain relief (drug tolerance).
- Dependence and addiction (see above – "How to identify a state of addiction?").
- Contact dermatitis (skin rash with inflammation that can include a burning feeling.
- Withdrawal symptoms that may be life-threatening in babies whose mothers used Butrans for a long period during pregnancy. See "Pregnancy and breastfeeding" in section 2.

If a side effect appears, if any of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult your doctor.

Side effects may be reported to the Ministry of Health by clicking on the link "Report on side effects following medicinal treatment" on the homepage of the Ministry of Health website (www.health.gov.il) which leads to an online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il/

5. How to store the medicine?

Avoid poisoning! This medicine especially, and any other medicine, should be stored in a closed place out of the reach and sight of 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) that appears on the package. The expiry date refers to the last day of that month.
- Storage conditions: store below 25°C. Make sure the patches are kept in their original aluminum sachet.
- Do not use the product if the patch or its packaging is damaged.
- Fold used patches in half with the sticky side inwards and discard in a safe place out of reach and sight of children. Consult the pharmacist on how to dispose of the patches. See also section 3 (d. – "Changing the patch").

6. Additional information

In addition to the active ingredient, the patches also contain:

Levulinic acid, oleyl oleate, povidone K90, polyacrylate adhesive (with and without cross linker), polyethylene terephthalates.

What does the medicine look like and what does the package contain?

In each package there are 2 beige-colored skin patches. Each patch is packed in a separate aluminum sachet.

Butrans 5: square patches with a size of 6.25 cm^2. "Butrans 5 µg/h" is printed in blue ink on the back of the patch.

Butrans 10: rectangle patches with a size of 12.5 cm^2. "Butrans 10 µg/h" is printed in blue ink on the back of the patch.

Butrans 15: rectangle patches with a size of 18.75 cm². "Butrans 15 µg/h" is printed in blue ink on the back of the patch.
Butrans 20: square patches with a size of 25 cm². "Butrans 20 µg/h" is printed in blue ink on the back of the patch.

Registration holder: Rafa Laboratories Ltd., PO Box 405, Jerusalem 9100301
Manufacturer: Lohmann Therapie Systeme (LTS), Germany.

Medicine registration number in the National Medicines Registry of the Ministry of Health:
Butrans 5: 1357031151
Butrans 10: 1357131152
Butrans 15: 1579934931
Butrans 20: 1357231153

Revised in August 2021 in accordance with the Ministry of Health guidelines.

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