

Sativex

Oromucosal spray

Composition:
Active ingredients and their concentration:
Each 1mL contains:
Delta-9- tetrahydrocannabinol 27 mg
Cannabidiol 25 mg

For list of inactive ingredients, please see section 6.

Read this entire leaflet carefully before using this medicine and each time this medicine is prescribed for you as new information may appear. This leaflet does not replace a consultation with your doctor regarding your medical condition or the treatment you receive. Share this important information with your family. This leaflet contains concise information about the medicine. If you have any further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It may harm them, even if you think that their illness is similar.

Sativex is not recommended for the use in children and adolescents under 18 years of age due to a lack of information regarding its safety and efficacy for these ages.

1. What is the Medicine Intended for?

- symptomatic relief in patients with moderate to severe spasticity due to Multiple Sclerosis, who do not respond adequately to other treatments and who demonstrate clinical improvement in spasticity related symptoms during an initial trial of therapy (4 weeks duration).
- as an add-on treatment for the symptomatic relief of neuropathic pain (pain caused by nerve damage) in Multiple Sclerosis adult patients.
- as add-on analgesic treatment in adult patients with advanced cancer who suffer from moderate to severe pain despite treatment with strong opiate medicines at the maximal dosage.

Therapeutic group: Cannabinoid analgesic

2. Before Using the Medicine

Do not use the medicine if:
<ul style="list-style-type: none">• you are breastfeeding.• you are hypersensitive (allergic) to cannabis extracts or to any other ingredients of this medicine.• you have experienced or you know of a family history of mental health problems such as: schizophrenia, psychosis or any other significant psychiatric disorders. This does not include depression due to Multiple Sclerosis.

Special warnings regarding the use of this medicine

- **Before treatment with Sativex tell the doctor if:**
 - you are pregnant or planning to become pregnant. Women and men must use an effective contraceptive method during treatment with Sativex and for at least three months after stopping treatment [see section "Pregnancy, Breastfeeding and Contraception (women and men)"].
 - you are under 18 years of age.
 - you suffer from liver or kidney disease.
 - you suffer from epilepsy or recurrent seizures.
 - you suffer from a severe cardiovascular disease such as: angina, previous heart attack, poorly controlled hypertension or a problem with your heart rate or heartbeat. Changes in heartbeat and blood pressure were observed after beginning the treatment and therefore caution is required when adjusting the dosage (titration period). Treatment with Sativex is not recommended in patients who suffer from severe cardiovascular diseases.
 - you have a history of medicine or substance abuse.
 - you are elderly, especially if you have problems performing everyday activities such as preparing food and hot beverages.
- If you are travelling to other countries, check that it is legal for you to be in possession of Sativex in those countries. This includes countries you are travelling through. Sativex is a controlled drug and its legal status may vary between countries. Driving while using Sativex may be illegal in some countries.

Tell the doctor or pharmacist if you are taking or have recently taken any other medicines, including non-prescription drugs and nutrition supplements. Especially if you are taking:

- hypnotics, sedatives and medicines with a sedating effect, as they may increase the effect of sedation and muscle relaxation and lead to an increased risk of falling and other accidents.
- muscle relaxants such as baclofen or benzodiazepines such as diazepam, since this may cause a reduction in muscle strength and power, leading to an increased risk of falls.
- when beginning or stopping treatment with itraconazole, ritonavir, clarithromycin – the dosage of Sativex may need to be adjusted.
- avoid concomitant use with rifampicin, carbamazepine, phenytoin, phenobarbital, the herbal medicine St. John's Wort (hypericum). If the use is essential, adjust the dosage of Sativex.

If you go to different doctor or to hospital, inform them about all the medicines you are taking.

Use of this medicine and food

You can use the product regardless of meals. However, using this product with a meal may affect the amount absorbed by your body. You should be consistent in using the product in the same way with respect to meals so you receive the same effect each use.

Use of this medicine and alcohol consumption

Avoid drinking alcoholic beverages during the treatment period of Sativex especially at the beginning of treatment or when changing the dosage. Drinking alcohol during the treatment period of Sativex may increase their effects (e.g. lead to a loss of balance or damage the ability to respond quickly) and therefore impair the ability to drive and operate machinery and increases the risk of falls and other accidents.

Pregnancy, Breastfeeding and Contraception (women and men)

- If you are pregnant, think you might be pregnant or planning to become pregnant, consult a doctor or pharmacist before taking this medicine.
- Do not use Sativex during pregnancy, unless instructed to do so by the doctor.
- Women and men must use a reliable contraceptive method during the treatment period of Sativex and for at least three months after stopping treatment.
- The medicine passes into breast milk. Do not use this medicine if you are breastfeeding.

Driving and Use of Machinery

- Do not drive or operate machinery when you first start taking Sativex and until you are stabilized on a regular daily dosage.
- The use of this medicine may cause dizziness and sleepiness, which may impair your judgement and performance of skilled tasks. It has also rarely been reported to cause a brief loss of consciousness.
- Do not drive while taking the medicine until you know how it affects you.
- Once you have adjusted to taking the medicine and your dosage is stable, still do not drive or operate machinery if Sativex causes effects such as sleepiness or dizziness that may influence your ability to perform these tasks.

Contact a doctor or pharmacist if you are not sure whether you can drive safely while using the medicine.

Important information about some of the ingredients of this medicine

- Sativex contains approximately 50% ethanol (alcohol) i.e. up to 40 mg per dose. The amount of alcohol in the maximum daily dose for most patients (12 sprays) is the same amount of alcohol as found in two teaspoons (10 ml) of beer or one teaspoon (5 ml) of wine. The medicine may be harmful for patients suffering from alcoholism.
- Sativex contains propylene glycol which may cause irritation. Symptoms of irritation include pain, itchiness, dry cough, sore throat.

3. How to Use this Medicine?

- Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure.
 - Sativex is intended to be sprayed in the mouth only, under the tongue or in the inside of the cheek. Do not spray in the throat in order to avoid inhaling the product.
 - Vary the location in the mouth where you spray Sativex in order to prevent tingling and discomfort in the mouth.
- Do not spray into the nose!**

The dosage and administration will be determined by the doctor only. Usual recommended dosage is:
Dosage adjustment:
The number of sprays each day depends on the individual. Each person needs a different number of sprays in order to provide the best relief, with the fewest unwanted effects.

- When you first start using Sativex, follow the days and times indicated in the table below until achieving the most suitable number of sprays for you. Your regular daily dose is determined after careful and gradual dose increase during the first few weeks of using Sativex.
- **Stop increasing the number of sprays when you find the best number of sprays that provides you with relief.** This process may take a few days up to two weeks.
- Do not use more than one spray at a time. Wait at least 15 minutes between sprays.
- Take the morning dose any time between waking-up and 12 noon, the afternoon/evening dose should be taken between 4 pm and bedtime.
- Do not over-exert yourself during the first few of days of treatment until you know how Sativex affects you.
- Once you have found the number of daily sprays that provide you with symptom relief, you can adjust the timing between them, depending on how you feel. Do not spray more than once at a time. Always be sure to space sprays at least 15 minutes apart. After adjusting the timing and number of sprays per day, continue with this schedule.
- Consult the doctor if you need more than 12 sprays a day in order to control the symptoms.
- If you suffer from bothersome side effects (usually dizziness) reduce the number of sprays or increase the time period between each spray until you feel the best symptom relief with the fewest unwanted effects.
- Follow these guidelines unless the doctor instructs you otherwise.

Day	Number of sprays in the morning (between waking-up and 12 noon)	Number of sprays in the evening (between 4 pm and bedtime)	Total number of sprays a day
Day 1	0	1	1
Day 2	0	1	1
Day 3	0	2	2
Day 4	0	2	2
Day 5	1	2	3
Day 6	1	3	4
Day 7	1	4	5
Day 8	2	4	6
Day 9	2	5	7
Day 10	3	5	8
Day 11	3	6	9
Day 12	4	6	10
Day 13	4	7	11
Day 14	5	7	12

Spasticity in Multiple Sclerosis:

For treatment of spasticity due to Multiple Sclerosis, the treatment must be initiated and supervised by a specialist only. If you do not experience an improvement in spasticity related symptoms following 4 weeks of treatment, consult the doctor.

How to Use:

When first opening a new container:

1. Take the spray out of the refrigerator (see section 5 "How to Store the Medicine?" regarding important information about storing Sativex).
2. Write the date of opening on the sticker provided with the spray. Stick the sticker on the spray so that you can check the date. Do not use a spray after it has been open for more than 6 weeks (42 days).
3. Shake the spray gently.
4. Remove the protective cap.
5. "Restarting the container":
Place the spray between the thumb and middle finger with the index finger placed on the actuator. While holding the spray in an upright position, firmly and quickly press two or three times into a tissue until a sufficient quantity of spray is dispensed (see diagram 1). These actuations "activate" the pump and help ensure that it works properly.
6. The medicine is now ready for regular use.

In regular use (there is no need to spray first on a tissue – this should only be performed when opening a new spray container):

1. Shake the spray gently before use.
2. Remove the protective cap.
3. Place the spray between the thumb and middle finger with the index finger placed on the actuator.
Hold the spray in an upright position and direct it into your mouth: under the tongue or on the inside of the cheek.
Hold your breath and press firmly and quickly.
Vary the area in the mouth to which you direct the spray each time in order to prevent tingling and discomfort in the same area (see diagram 2).
4. Do not use more than one spray each time, even if you feel that you received a small amount of spray.
4. Replace the protective cap.

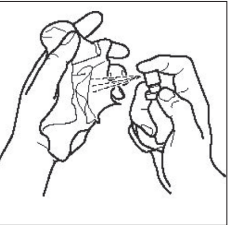


Diagram 1

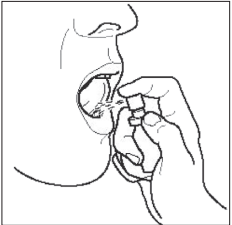


Diagram 2

Do not exceed the recommended dose.

- Keep the spray away from the eyes. If the spray comes into contact with your eyes or skin, wash the area immediately with plenty of water.
- Sativex is intended for application in the mouth only! Do not inhale the spray.
- Do not spray near children or pets.
- Do not use the spray near an open flame or heat source.
- After the 3 priming sprays (the sprays intended to restart the container), the container contains up to 90 measured sprays. As the container empties, the noise of the spray action changes and you may feel a different sensation in your mouth. At this stage, open a new container of the medicine.

Tests and Follow Up

If you are being treated with Sativex for a prolonged period, the lining of the mouth must be examined regularly.

If you have accidentally taken a higher dosage you may experience severe intoxication reaction that include dizziness, sleepiness, confusion, hallucinations (seeing or hearing things that are not there) and believing things that are not true (delusions), anxiety or paranoia (increased anxiety or fear), changes in heart rate accompanied by hypotension (feel dizzy upon standing).
If you have taken an overdose or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you.
Following an overdose, set an appointment with the doctor for follow-up.

If you forget to take this medicine

If you forget to take a dose, take another dose as soon as you remember or feel the need to. Do not take a double dose to compensate for a forgotten one.

Continue with the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop taking this medicine without consulting a doctor.

If you stop taking this medicine consult a doctor before deciding to stop using Sativex after regular use. Sudden cessation of Sativex use may affect sleep, appetite or feelings for a short time. The spasticity usually returns gradually with cessation of use of the medicine.

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

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

4. Side Effects

Like all medicines, Sativex may cause side effects in some users. Do not be alarmed while reading the list of side effects, you may not suffer from any of them.
Side effects are most common at the beginning of the treatment. These side effects are usually quite mild and resolve within a few days even if the treatment is continued. If you experience the following side effects, reduce the number of sprays or stop the use of Sativex until you feel better. When you start using the medicine again, start by using the number of sprays that did not cause the unwanted side effects.
The number of side effects that occur at the beginning of the treatment can be significantly reduced by following the instructions for increasing the dosage (see section 3 "How to Use this Medicine").

Stop the use of this medicine and refer to a doctor if any of the following side effects appear:

- difficulty speaking
- blurred vision
- memory or concentration disturbances
- feeling over-excited (euphoria) or losing touch with reality
- feeling depressed or confused
- hallucinations (seeing or hearing things that are not there)
- believing ideas that are not true
- feeling that other people are against you
- suicidal thoughts
- changes in heart rate, pulse or blood pressure

Very common side effects:

- dizziness or tiredness

Common side effects:

- (affects less than 1 in 10 patients)
- **Nutrition disorders:** decrease in appetite, increase in appetite.
- **Psychiatric disorders:** depression or confusion, disorientation, feeling of euphoria, losing touch with reality.
- **Central nervous system disorders:** forgetfulness (amnesia), balance disorder, attention deficit disorder, pronunciation impairment, changed sense of taste, lethargy, memory impairment, somnolence.
- **Gastrointestinal disorders:** constipation, diarrhoea, dry mouth, pain of the tongue, nausea, vomiting, mouth problems including burning sensation, pain, discomfort or ulcers.
- **General disturbances and administration site effects:** application site pain, lack of energy or weakness (asthenia), feeling abnormal, feeling drunk, feeling or being sick. Sativex may also cause white spots on the tongue (leucoplakia).
- **Other:** blurred vision, dizziness (vertigo), falls.

Uncommon side effects:

- (affects less than 1 in 100 patients)
- **Central nervous system disorders:** hallucinations, anxiety, delusions, feeling that others are against you, suicidal thoughts.
- **Cardiac disorders:** strong heartbeat (palpitations), rapid heart rate (tachycardia).
- **Gastrointestinal disorders:** abdominal pain (upper abdomen), oral mucosal discolouration, oral mucosal disorders, inflammation (red and swollen mouth) and peeling of the oral mucosa – do not keep spraying onto these areas, tooth discolouration.
- **Other:** inflammation of the throat (pharyngitis), hypertension, fainting, irritated or sore throat, irritation at the spraying area.

Clinical studies show an increase in the incidence of urinary retention combined with urinary tract infections in cancer patients treated with Sativex compared to patients who did not take Sativex, therefore caution must be taken to prevent urinary tract infections.

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

5. How to Store the Medicine?

- Avoid poisoning! This medicine and all other medicines must be stored in a safe 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 a doctor.
- Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.
- Store the containers in an upright position.
- Before opening, store in the refrigerator at a temperature of 2-8°C.
- Once opened (first spray), use the container within 42 days.
- Once opened, refrigeration is unnecessary, but the medicine should be stored at a temperature below 25°C.
- Shake the container gently before use.
- This product is flammable. Replace cap after use.
- Do not light a cigarette or become exposed to fire until the product has completely dried.
- Protect from light and keep the medicine away from heat and fire sources. Store in a safe place. Do not give your medicine to anyone else.
- If you experience one or more side effects listed above, or if you have suffered a different side effect, please report side effects using the online form with the following link:
<http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic%40moh.health.gov.il> or to: ADR@MOH.health.gov.il as well as to Neopharm by email: DrugSafety@neophamisrael.com
- Medicines should not be disposed of via wastewater or household waste. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help to protect the environment.

6. Additional Information

In addition to the active ingredients, this medicine also contains:
Ethanol anhydrous, Propylene glycol, Peppermint oil (flavour)

What the medicine looks like and what the package contains:

Yellow-brown liquid in a 10 ml spray container with a pump. The pump is protected by a plastic cap.
Each Sativex package contains 1, 2, 3, 4, 5, 6, 10 or 12 spray containers.
Not all pack sizes may be marketed.

Registration holder and address: Neopharm Scientific Ltd., POB 7063 Petach Tikva 49170.



Manufacturer and address: GW Pharma Ltd., Cambridge, UK.

Drug registration number at the national medicines registry of the Ministry of Health: 147-48-33290-00

This leaflet was checked and approved by the Ministry of Health in 03/2015

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