

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

This medicine is dispensed with a doctor's prescription only

## **Sativex**

### **Oromucosal spray**

#### **Composition:**

##### **Active ingredients and their concentration:**

Each 1mL contains:

Delta-9- tetrahydrocannabinol 27 mg

Cannabidiol 25 mg

Inactive ingredients and allergens: See section 6 'Additional information' and section 2 under 'Important information about some of the ingredients of this medicine'.

**Read this entire leaflet carefully before using this medicine.** 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.

#### **1. What is the Medicine Intended for?**

symptomatic relief in patients with moderate to severe spasticity due to multiple sclerosis (MS), who do not respond adequately to other treatments and who demonstrate at least 20% clinical improvement in spasticity related symptoms during an initial trial of therapy (4 weeks duration).

**Therapeutic group:** Cannabinoid analgesic

Spasticity means there is an increase in 'muscle tone' which makes the muscles feel more stiff or rigid. This means it is more difficult than normal to move the muscle.

Sativex is used when other medicines have not helped your muscle stiffness.

#### **2. Before Using the Medicine**

**Do not use the medicine if:**

- you are hypersensitive (allergic) to cannabis extracts or to any other ingredients of this medicine (listed in section 6).
- you or anyone directly related to you has any mental health problems such as schizophrenia, psychosis or other significant psychiatric disorders. This does not include depression due to your multiple sclerosis.
- you are breast-feeding.

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

- **Before treatment with Sativex tell your doctor if:**
  - you are pregnant or plan to become pregnant.
  - you are under 18 years of age.
  - you have epilepsy or regular fits (seizures).
  - you have kidney problems.

- You have moderate to severe liver problems.
- you have a serious heart problem such as: angina, a previous heart attack, poorly controlled high blood pressure or a problem with your heart rate or heartbeat.
- you are elderly, especially if you have problems doing everyday activities such as making hot food and drinks.
- you have previously abused any drug or substance.

Whether male or female you must use a reliable contraceptive method while using this medicine (see also “Pregnancy, breast-feeding and contraception (men and women)”)

### **Children and adolescents**

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.

### **Other medicines and Sativex**

**If you are taking or have recently taken any other medicines, including non-prescription drugs and nutrition supplements, tell your doctor or pharmacist.**

Especially if you are taking:

- anxiety or sleeping problems (sedatives/hypnotics like benzodiazepine, for example diazepam or triazolam; other sedatives, for example zopiclone, zolpidem, buspirone, St John’s Wort (a herbal preparation)).
- muscle spasms (such as baclofen) bacterial infections (antibiotics such as rifampicin, clarithromycin).
- epilepsy or nerve pain (such as phenytoin, phenobarbital, carbamazepine).
- high cholesterol (known as statins; for example atorvastatin or simvastatin)
- fungal infections (such as itraconazole, fluconazole and ketoconazole)
- HIV infection (for example ritonavir)
- thinning your blood (known as coumarins; for example warfarin)
- heart problems (known as betablockers, for example bisoprolol, propranolol)
- corticosteroids used for inflammation (such as hydrocortisone, beclomethasone, prednisolone)
- Some hormone medicines used for contraception or some types of cancer (such as ethinyloestradiol, levonorgestrel or dydrogesterone)
- anaesthesia to put you to sleep before an operation/surgery relaxing muscles before surgery (such as propofol)

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 Sativex with or without food (but see section 3 below “How to use Sativex”).

### **Use of this medicine and alcohol consumption**

In general, alcoholic beverages should be avoided whilst using Sativex especially at the beginning of treatment or when changing dose. If you do drink alcohol while using Sativex, be aware that using Sativex and alcohol together may increase their effects (such as loss of balance or ability to respond quickly) which could increase the risk of falls and other accidents.

### **Pregnancy, breastfeeding and contraception (women and men)**

- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.
- Do not use Sativex during pregnancy, unless advised to by your doctor. Sativex may affect the way hormonal birth control methods, such as the "pill" or contraceptive implants, work. This means you should use an additional type of contraception.

Whether male or female you must use a reliable barrier contraceptive method such as a condom, diaphragm or cap while using this medicine. Keep doing this for at least 3 months after your treatment has stopped.

- Do not use Sativex while breast-feeding.

### **Driving and use of machinery**

- You must not drive or use machinery when you first start to take Sativex and until you are established on a stable daily dose.
- Sativex may cause you to feel sleepy or dizzy, which may impair your judgement and performance of skilled tasks. It has also rarely been reported to cause a brief loss of consciousness.
- Once you are more used to taking Sativex and your dose is stable, you should still not drive or use machinery if Sativex causes effects such as sleepiness or dizziness that could impair your ability to perform these tasks. If you are not sure, do not drive or operate machines.

The medicine can affect your ability to drive as it may make you sleepy or dizzy.

**According to the Israeli transport regulations and the narcotics ordinance, driving is forbidden during Sativex use**

### **Foreign travel with Sativex**

Before going abroad, check that it is legal for you to take this medicine. This includes any country you are travelling through.

- Sativex is a Controlled Drug and its legal status will vary between countries.
- Driving while taking Sativex might be illegal in some countries.

### **Important information about some of the ingredients of this medicine**

- Sativex contains up to 40 mg of ethanol (alcohol) per dose. The amount of alcohol in the maximum daily dose for most people (12 sprays) is about the same as found in two teaspoons (10 ml) of beer and about one teaspoon (5 ml) of wine. The small amount of alcohol in this medicine will not have any noticeable effects.
- This medicine contains propylene glycol which may cause irritation. Each 100 microlitre spray contains 52 mg propylene glycol

### **3. How to Use this Medicine?**

Always use this medicine according to your doctor's instructions. Check with the doctor or pharmacist if you are not sure about your dosage and method of administration.

Only use Sativex in your mouth - in the inside of the cheek or under the tongue.

Taking Sativex with food can affect the amount your body takes in. You should try, as far as possible, to take Sativex the same way in relation to food each time, so you get the same effect each time.

**The dosage and administration will be determined by the doctor only. The recommended dosage is usually:**

Working out how much to use:

The number of sprays you need each day depends on you as an individual. Each person needs a different number of sprays to give them the best relief from their muscle stiffness, with the fewest unwanted effects.

- When you first start using Sativex, you need to follow the days and times in the following table until you find the best number of sprays for you.
- **Stop increasing your sprays when you find the best number of sprays for you.** This may only take a few days or it may take up to 2 weeks. Aim to use this number of sprays each day. You can then spread your sprays evenly over the whole day.
- Do not use more than one spray at a time. Always leave at least 15 minutes between sprays.
- Do not over-exert yourself during the first couple of days of using Sativex until you know how it affects you.
- If you start to feel unwanted effects (usually dizziness) use one less spray each day until you find the best symptom relief with the fewest unwanted effects.
- When you find the best number of sprays for you, aim to use this number each day. You can then spread your sprays out evenly over the whole day, in a way that suits you. Still leave at least 15 minutes between sprays.

<b>Number of sprays</b>			
<b>Day</b>	<b>Morning</b> (between waking-up and 12 noon)	<b>Evening</b> (between 4 pm and bedtime)	<b>Total sprays each day</b>
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

Do not use more than 12 sprays in one day, unless your doctor tells you to.

**Your 4 week trial of Sativex:**

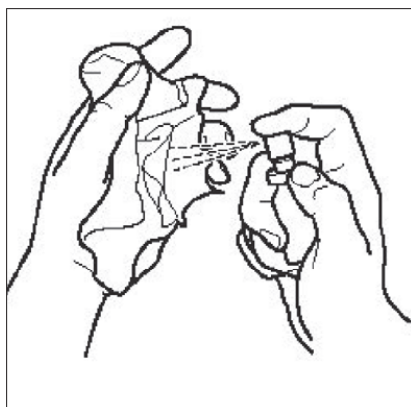
Only a specialist doctor can start you on treatment with Sativex.

- Before you start using Sativex your specialist doctor will do an assessment. This is to see how bad your muscle stiffness is. They will look at how well other treatments have worked.
- You will then have 4 week trial of Sativex. After this, your specialist doctor will do another assessment to see whether Sativex is helping you.
- Only if you have shown a significant improvement in your spasticity related symptoms after these 4 weeks should you continue to be treated with Sativex.

## **How to Use:**

### Opening your spray and getting it ready to use:

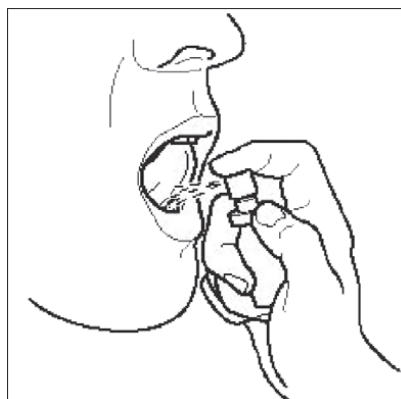
1. Take the spray out of the refrigerator (see section 5 for important information about storing Sativex).
2. Write the date that you open your spray on the sticker provided with the spray. Stick the sticker on the spray so that you can check the date. Do not use a spray after it has been open for more than 6 weeks (42 days).
3. Shake the spray container gently before use.
4. Remove the protective cap.
5. Hold the spray between your thumb and second finger. Put your first finger on the nozzle.
6. Hold the spray upright, then practice spraying into a tissue 2 or 3 times until a fine spray appears (see diagram 1). These sprays "prime" the pump and make sure it is working properly.
7. The spray is now ready to use. You will not need to do any more priming sprays until you open a new spray container.



**Diagram 1**

### Using your spray:

1. Hold the spray between your thumb and second finger. Put your first finger on the nozzle.
2. Hold it upright and point into your mouth. Point the nozzle under your tongue or onto the inside of your cheek. Change the area in your mouth where you spray each time. This helps to stop discomfort in one place (see diagram 2).
3. Press the nozzle down firmly. Do not take more than one spray a time, even if you feel that you only got a small amount of spray.
4. Replace the protective cap.



**Diagram 2**

**Do not exceed the recommended dose.**

If you get spray in your eyes by accident, wash them as soon as possible with water.

- Do not breathe in the spray.
- Do not spray near children or pets.
- Do not use the spray near naked flames or heat source.

**If you use more Sativex than you should**

If you accidentally use more of this medicine than you normally do, you may:

- See or hear things that are not there (hallucinations).
- Feel dizzy, sleepy or confused
- Feel your heart rate change.
- Please tell your doctor or pharmacist if you used more Sativex than you should

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.

**If you forget to use Sativex**

- If you forget to take a dose, use a spray as soon as you remember or when you feel you need a spray.
- Do not use 2 sprays at the same time to make up for a missed spray.

**Knowing if your spray is nearly empty**

After the 3 priming sprays, your spray contains up to 90 measured sprays. When the spray is becoming empty, the noise of the spray action change. You may also find the spray feels different in your mouth. This is because your spray is nearly empty. When this happens you should open a new spray container.

**If you stop using Sativex**

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 using your medicine suddenly your sleep, appetite or feelings might be affected for a short time. Your muscle stiffness usually comes back gradually if you stop using Sativex.

**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 your doctor or pharmacist.**

**4. Side Effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them. Do not be alarmed while reading the list of side effects, you may not suffer from any of them.

**Stop the use of this medicine and refer immediately to a doctor or go to a hospital straight away if any of the following serious side effects appear as you will need to be monitored until the symptoms stop:**

- seeing or hearing things that are not there (hallucinations)
- believing ideas that are not true
- feeling that other people are against you
- thoughts of suicide
- feeling depressed or confused
- feeling over-excited or losing touch with reality

The following side effects are more likely when you start your treatment. In most cases side effects are quite mild and they generally wear off within a few days.

- If you get any of the following side effects, use less sprays or stop using Sativex until you feel normal again.
- When you start using the medicine again, to back to the number of sprays where you did not feel these unwanted side effects.

**Very common side effects:** (affect more than 1 in 10 patients)

- Feeling dizzy or tired

**Common side effects:** (affect less than 1 in 10 patients)

- Problems with your memory or having trouble concentrating.
- Feeling sleepy or giddy.
- Blurred vision.
- Difficulty speaking.
- Eating more or less than usual.
- Changed sense of taste or a dry mouth.
- Constipation or diarrhoea.
- Feeling or being sick.
- Mouth problems, including burning, pain or mouth ulcers.
- Lack of energy or feeling weak or generally unwell.
- Feeling abnormal or drunk.
- Loss of balance or falling over.

**Uncommon side effects:** (affect less than 1 in 100 patients)

- Fainting.
- Changes in pulse rate, heart rate or blood pressure.
- Sore throat or throat irritation.
- Tummy pain.
- Mouth or teeth changing colour.
- Irritation where Sativex is sprayed.
- Red and swollen mouth or peeling inside it. Do not keep spraying onto these areas.

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

**Reporting of side effects**

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” that appears on the homepage of the Ministry of Health’s website ([www.health.gov.il](http://www.health.gov.il)) which links to an online form for reporting side effects, or by the following link: <https://sideeffects.health.gov.il/>

In addition, you can report by emailing the Registration Holder’s Patient Safety Unit at: [drugsafety@neopharmgroup.com](mailto:drugsafety@neopharmgroup.com)

## **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.

### **Storage conditions:**

- 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.

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.

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 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 contents of the package:**

Yellow-brown liquid in a 10 ml glass spray container with a pump. The pump is protected with 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., Hashiloach 6, POB 7063 Petach Tikva 4917001.

**Manufacturer's name and address:** GW Pharma Ltd., Sovereign House, Vision Park, Histon, Cambridge, CB24 9BZ, UK.

**Registration number of the medicine in the Ministry of Health's National Drug Registry:** 147-48-33290

Revised in June 2022 according to MOH's guidelines.