

Epidiolex 100 mg/mL Cannabidiol

Oral solution

Active ingredient:

Each 1 mL of Epidiolex oral solution contains 100 mg of cannabidiol.

For the list of excipients of the medicine, please see section 2: "Important information about some of the Epidiolex ingredients" and section 6: "Additional information".

Read the entire leaflet carefully before you start using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, contact your physician or pharmacist.

This medicine has been prescribed to treat your/your child's illness. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

1. What is the medicine intended for?

Epidiolex is indicated for use as adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), or tuberous sclerosis complex (TSC) in patients 1 year of age and older.

Pharmacotherapeutic group: antiepileptics, other antiepileptics.

2. Before using this medicine

Do not take Epidiolex if:

- You/your child are hypersensitive (allergic) to cannabidiol, to other cannabidiol derivatives or to any of the other ingredients of this medicine (listed in section 6). If you are not sure, talk to your physician or pharmacist before taking Epidiolex.

Special warnings regarding the use of this medicine

Talk to your physician or pharmacist before taking Epidiolex if:

- You/your child have or have had liver problems, as your physician may need to change the dose of Epidiolex or may decide that Epidiolex is not appropriate for you.
- The physician may also do blood tests to check the liver before initiation of this medicine and during treatment, as Epidiolex can cause liver problems. If the liver is not working properly, the treatment may need to be stopped.
- You/your child are taking any other antiepileptic medication, especially valproate or clobazam. This could result in altering liver function and the efficacy of treatment. The physician might decide to change the dose of Epidiolex or the other antiepileptic medications.
- You/your child are taking any other antiepileptic medication, especially in combination with other antiepileptic drugs, such as clobazam, or other sedative medicines or alcohol. Epidiolex can make one feel sleepy in combination with these drugs. Do not drive, operate machinery, or take part in activities that require you/your child to be alert and have fine motor control, such as cycling, until you know how Epidiolex affects you/your child.
- You notice unusual changes in your mood or your child's mood or behaviour or have thoughts of harming or killing yourself/themself. Contact your physician or go to a hospital straight away.
- You notice skin rash, itchiness, swelling of the skin or redness of the skin. These symptoms might be related to hypersensitivity to Epidiolex. Contact your physician or go to a hospital straight away.

Children and adolescents

Epidiolex is not recommended for use in children under 1 year of age with LGS/DS/TSC.

Elderly people

Clinical trials of Epidiolex in the treatment of seizures associated with LGS, DS, and TSC have not included a sufficient number of patients aged above 55 years to determine whether or not they respond differently from younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Laboratory tests and follow-up

Your physician might perform blood tests to check liver function:

- before the start of treatment with Epidiolex
- with additional testing dependent on Epidiolex dose and the dose of other antiepileptic medicines you are taking.

Drug-drug interactions

Tell your physician or pharmacist if you or your child are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements. Taking Epidiolex with certain other medicines may cause side effects, affect how other medicines work, or affect how Epidiolex works.

In particular, your physician may need to adjust your Epidiolex dose if you take the following medicines:

- Other epilepsy medicines, such as carbamazepine, clobazam, lamotrigine, lorazepam, midazolam, phenytoin, stiripentol and valproate that are used to treat seizures
- mTOR or calcineurin inhibitors, such as everolimus and tacrolimus
- Caffeine (a medicine for infants who need help breathing)
- Theophylline (a medicine used to treat asthma)
- Bupropion (a medicine used to help stop smoking or for treating obesity)
- Efavirenz (a medicine used to treat HIV/AIDS)
- Diflunisal, morphine (medicines used to treat pain)
- Propofol (an anaesthetic used for people undergoing surgery)
- Fenofibrate, gemfibrozil (medicines used to reduce cholesterol/lipids)
- Diazepam (used for treating anxiety)

Taking this medicine with food

Food affects the absorption of the medicine into your bloodstream. Epidiolex should always be taken according to the physician's instructions and consistently either with or without food, including high-fat meals (such as a ketogenic diet).

Using the medicine with alcohol

Combining this medicine with alcohol is not recommended.

Alcohol could potentiate the sleepiness and sedation effects of Epidiolex.

Pregnancy, breastfeeding and fertility

If you are pregnant, think you may be pregnant, or are planning to have a baby, ask your physician or pharmacist for advice before taking this medicine. You should not take Epidiolex while you are pregnant unless the physician has decided that the benefits of the medicine outweigh the potential risks.

There are no data on the presence of cannabidiol or its metabolites in human breast milk, the effects on the breastfed infant, or the effects on milk production.

Consult with your physician before taking the medicine if you are breastfeeding.

There is no available data on the effect of this medicine on human fertility.

Driving and using machines

You may feel sleepy, dizzy or tired while taking Epidiolex. These effects are more likely to occur at the start of the treatment or after a dose increase. Do not drive, cycle or use any tools or machines until you know how the medicine affects you. Children should be warned against riding bicycles or playing close to the road and the like.

The medicine can affect your ability to drive, cycle or use any tools or machines as it may make you sleepy or dizzy.

According to the Israeli transport regulations and the narcotics ordinance, driving is forbidden during Epidiolex use.

Important information about some of the Epidiolex ingredients

Epidiolex contains refined sesame oil which may rarely cause severe allergic reactions.

This medicine contains 79 mg of dehydrated alcohol (ethanol anhydrous) in each mL of the solution; i.e. up to 691.3 mg per maximal dose (12.4 mg/kg) for an adult weighing 70 kg.

The amount of ethanol in this medicine is equivalent to 17 mL of beer or 7 mL of wine per dose for an adult weighing 70 kg.

3. How to use the medicine?

Always take this medicine exactly as instructed by the physician. Check with your physician or pharmacist if you are not sure.

The dosage and treatment regimen will be determined only by the physician.

Epidiolex is to be administered orally. The physician will calculate the dose according to the body weight. You/your child may start on a low dose that the physician gradually increases over time. Contact your physician if you are unsure of your dose or that of your child or if you think the dose needs to be changed.

The commonly recommended dosage for seizures associated with Lennox-Gastaut syndrome or Dravet syndrome is:

- The starting dosage is 2.5 mg/kg twice daily (5 mg/kg/day).
- After one week, the dosage can be increased to a maintenance dosage of 5 mg/kg twice daily (10 mg/kg/day).
- The physician might increase the daily dose up to 10 mg/kg twice daily (20 mg/kg/day).

The commonly recommended dosage for seizures associated with tuberous sclerosis complex is:

- The starting dosage is 2.5 mg/kg twice daily (5 mg/kg/day).
- After one week, the dosage can be increased in weekly increments of 2.5 mg/kg twice daily (5 mg/kg/day), as tolerated.
- The physician might increase the daily dose to the recommended maintenance dosage of 12.5 mg/kg twice daily (25 mg/kg/day).

Two calibrated measuring devices (1 mL and 5 mL oral syringes) are provided within the package. If your dose of Epidiolex is 1 mL or less, use the 1 mL syringes to take your medicine. A household teaspoon or tablespoon is not an adequate measuring device.

Taking Epidiolex with food can increase the amount of medicine the body takes in. Try, as far as possible, to take Epidiolex consistently either with or without food, and according to your daily routine, so you get the same effect each time.

Patients with liver problems

Tell your physician if you/your child have liver problems, because the physician may need to adjust the dose.

Do not exceed the recommended dose.

Do not reduce the dose or stop taking this medicine unless the physician tells you to.

Epidiolex is a long term treatment. Keep taking Epidiolex until your physician tells you to stop.

If you have accidentally taken a higher dosage

If you have taken more Epidiolex than you should, consult your physician immediately.

If a child consumed an overdose of Epidiolex or consumed Epidiolex by mistake, consult immediately with your physician or attend the emergency room at the nearest hospital and bring the medicine with you.

Signs of taking more Epidiolex than you should include diarrhoea and sleepiness.

If you/your child forget to take Epidiolex

If you/your child forget to take a dose, do not take a double dose to make up for a forgotten dose. Take the next dose at the regular time. If you/your child have missed many doses, please talk to your physician about the correct dose to take.

If you/your child stop taking Epidiolex

Do not stop taking this medicine unless your physician tells you to do so.

If the physician asks to stop taking this medicine, the dose will be lowered gradually.

Gradual discontinuation helps minimize the risk of increased seizure frequency and status epilepticus.

One should continue taking the medicine as recommended by the physician.

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 on the use of this medicine, ask your physician or pharmacist.

4. Side effects

Like all medicines, Epidiolex can cause side effects in some users.

Do not be alarmed by reading the list of side effects. You/your child may not experience any of them.

The following side effects could be **very important** and require special attention in the case that you/your child are a patient with LGS/DS/TSC:

- High liver enzymes (transaminases elevations) seen in blood tests, which can be a sign of liver injury, have been reported in patients receiving Epidiolex.
- People taking this medicine can have thoughts of harming or killing themselves. If these thoughts start at any time, contact the physician.
- Sleepiness is generally reported more common early in treatment and may diminish with continued treatment. Do not drive, operate machinery, or take part in activities that require alertness.
- Hypersensitivity reactions (skin rash, itchiness, swelling of the skin or redness of the skin) require immediate contact with the physician.
- Stopping a seizure medicine such as Epidiolex suddenly can cause seizures more often or seizures that do not stop (status epilepticus).

Call your healthcare provider right away if

- you/your child develop symptoms of liver problems during treatment such as: loss of appetite, nausea, vomiting, fever, feeling unwell, unusual tiredness, yellowing of the skin or the whites of the eyes (jaundice), itching, unusual darkening of the urine, right upper stomach area pain or discomfort.
- you/your child have the following symptoms associated with suicidal thoughts or actions: thoughts about suicide or dying, attempt to commit suicide, new or worse depression, new or worse anxiety, feeling agitated or restless, panic attacks, trouble sleeping (insomnia), new or worse irritability, acting aggressive, being angry or violent; acting on dangerous impulses, an extreme increase in activity and talking (mania), other unusual changes in behaviour or mood.

You/your child may get the following side effects when taking this medicine for seizures associated with LGS/DS.

Tell the physician if any of the following occurs:

Very common side effects (may affect more than 1 in 10 people):

- feeling drowsy or sleepy
- decreased appetite
- diarrhoea
- blood tests showing increases in levels of certain liver enzymes (which may be signs of liver damage)
- feeling tired
- rash
- difficulty in sleeping
- infections (including viral)

Common side effects (may affect more than 1 in 100 people):

- lack of energy
- pneumonia
- shaking of the body or parts of it
- feeling bad-tempered (irritable, aggressive)
- abdominal pain or discomfort
- weight decrease
- drooling
- agitation
- infection (fungal)
- stomach (gut) infection
- low oxygen levels in the blood

You/your child may get the following side effects with this medicine for seizures associated with TSC.

Tell the physician if any of the following occurs:

Very common side effects (may affect more than 1 in 10 people):

- diarrhoea
- blood tests showing increases in levels of certain liver enzymes (which may be signs of liver damage)
- decreased appetite
- feeling drowsy or sleepy
- fever
- vomiting

Common side effects (may affect more than 1 in 100 people):

- anaemia (low red blood cell count)
- platelet count decreased
- low white blood cell count
- feeling sick
- stomach (gut) infection
- weight decrease
- shaking of the body or parts of it
- weakness and lack of energy
- ear infection
- urinary tract infection
- pneumonia
- rash
- runny nose

If a side effect appears or if any side effect gets worse or if you suffer from a side effect not mentioned in the leaflet, you should consult the physician.

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) which links to an online form for reporting side effects, or by the following link:

<https://sideeffects.health.gov.il/>

and by emailing the Registration Holder's Patient Safety Unit at:

drugsafety@neopharmgroup.com

5. How to store the medicine

- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the sight and reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without specific instruction from the physician.
- Do not use the medicine after the expiration date (exp. date) appearing on the bottle's label. The expiration date refers to the last day of that month.
- This medicine may be used for 12 weeks after opening then discard any remainder. No special storage conditions apply after opening.
- There are no special storage conditions for this product. It is recommended to store at room temperature. Do not freeze. Keep the cap tightly closed.
- 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. Additional information

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

Refined sesame oil, ethanol anhydrous (dehydrated alcohol) (7.9% w/v), sucralose, and strawberry flavor

What Epidiolex looks like and contents of the pack

Epidiolex is a clear colorless to yellow solution, supplied in an amber glass bottle containing 100 mL of oral solution.

The medicine is packaged in a carton box containing two 1 mL calibrated oral dosing syringes, two 5 mL calibrated oral dosing syringes and two bottle adapters for using these syringes.

Instructions for use:

Be sure that you read, understand and follow these instructions carefully to ensure proper dosing of the oral solution.

Important:

- Follow your physician's instructions for the dose of Epidiolex you should take or give.
- Ask your physician, healthcare provider or pharmacist if you are not sure how to prepare, take, or give the prescribed dose of Epidiolex.
- Always use the oral syringe provided with Epidiolex to make sure you measure the right amount of Epidiolex.
- Do not use Epidiolex after the expiration date on the package and on each bottle.
- Use Epidiolex within 12 weeks of first opening the bottle.
- After 12 weeks, safely throw away (dispose of) any Epidiolex that has not been used.

Each package contains:

Child-resistant cap



2 bottle adapters



1 bottle of Epidiolex oral solution (100 mg/mL)



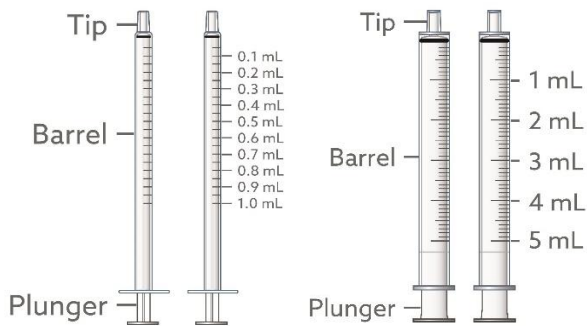
Please note expiration date

2 reusable 1 mL oral syringes and 2 reusable 5 mL oral syringes:

If your/your child's dose of Epidiolex is 1 mL or less, use the 1 mL syringes to take your medicine.

For each syringe size:

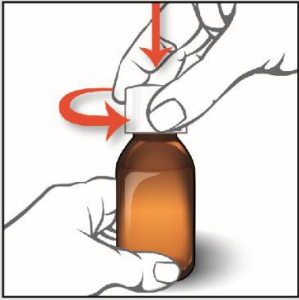
- 1 syringe to take or give the dose of Epidiolex
- 1 extra syringe (included as a spare if needed)



Note: If you lose or damage an oral syringe, or cannot read the markings, use the spare syringe.

Prepare the bottle to use Epidiolex for the first time

1. Remove the child-resistant cap by pushing down while turning the cap to the left (counter-clockwise).



2. Push the bottle adapter firmly into the bottle. **Make sure the bottle adapter is fully inserted.** If not fully inserted, small parts such as the bottle adapter may become a choking hazard for children and pets.

Note: Do not remove the bottle adapter from the bottle after it has been inserted.



Prepare the dose

Your physician will tell you how much Epidiolex to take or give.

3. Use this table to measure the total dose of Epidiolex to be given.

Dose

1 mL or less
More than 1 mL and less than 5 mL
More than 5 mL

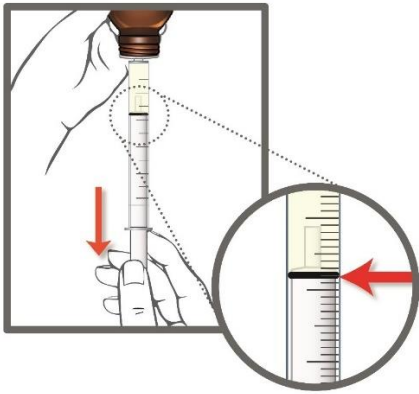
How to measure

Use the 1 mL oral syringe **1 time**
Use the 5 mL oral syringe **1 time**
Use the 5 mL oral syringe more than 1 time

4. Push the plunger all the way down and insert the tip of the oral syringe fully into the bottle adapter. With the oral syringe in place, turn the bottle upside down.



5. Slowly pull the plunger of the oral syringe to withdraw the dose of Epidiolex needed. See **Step 3** for how to measure the total dose of Epidiolex. **Line up** the end of the plunger with the marking for your/your child's dose of Epidiolex.



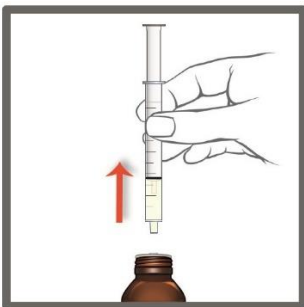
What to do if you see air bubbles:

If there are air bubbles in the oral syringe, keep the bottle upside down and push the plunger so that all of the liquid flows back into the bottle. Repeat **Step 5** until the air bubbles are gone.

6. When you have measured the correct dose of Epidiolex, leave the oral syringe in the bottle adapter and turn the bottle right side up.

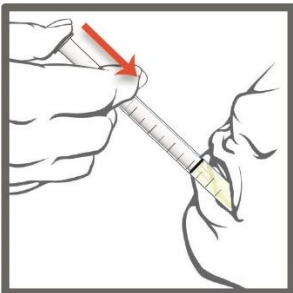


7. Carefully remove the oral syringe from the bottle adapter.



Give Epidiolex

8. Place the tip of the oral syringe against the inside of the cheek and gently push the plunger until all of the Epidiolex in the syringe is given.



Do not forcefully push on the plunger.

Do not direct the medicine to the back of the mouth or throat. This may cause choking.

If the dose of Epidiolex prescribed by the physician is more than 5 mL, repeat **steps 4 through 8** to complete the dose.

For example:

If your dose of Epidiolex is 8 mL, withdraw 5 mL of medicine into the syringe and give the medicine. Insert the tip of the oral syringe back into the bottle adapter and withdraw 3 mL of medicine. Give the medicine to receive a total dose of 8 mL.

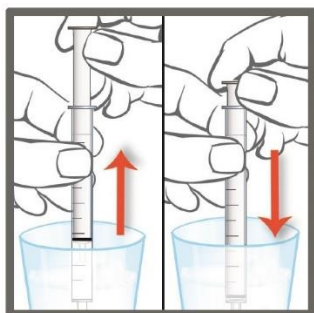
Clean up

9. Screw the child-resistant cap back on the bottle tightly by turning the cap to the right (clockwise).

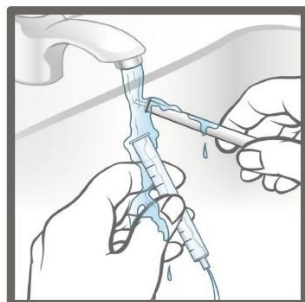


Do not remove the bottle adapter. The cap will fit over it.

10. Fill a cup with warm soapy water and clean the oral syringe by drawing water in and out of the syringe using the plunger.

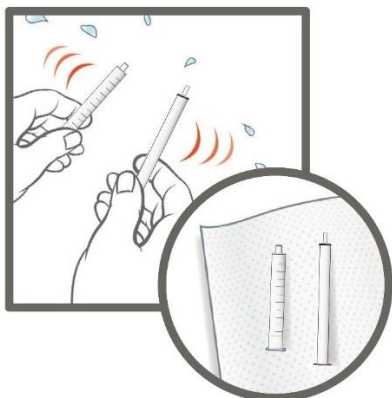


11. Remove the plunger from the barrel of the oral syringe and rinse both parts under tap water.



Do not wash the oral syringe in the dishwasher.

12. Shake off any extra water from the plunger and oral syringe barrel **and allow them to air dry until the next use.**



Make sure the oral syringe is completely dry before the next use. If there is water inside the syringe, it could cause the oil-based medicine to look cloudy.

Do not throw away the oral syringe.

Registration holder: Neopharm Ltd., 6 Hashiloach St., POB 7063,
Petach Tiqva 4917001, Israel

Manufacturer: GW Pharma Ltd., UK
Kent Science Park, Sittingbourne, Kent, ME9 8AG, UK

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 167-13-36105-00

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Epidiolex Sol PIL vs 03B