

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Synarel® 2 mg/mL Nasal solution



Active ingredient
nafarelin acetate 2 mg/mL
Each actuation releases 200 mcg nafarelin

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

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

This medicine is for use in women only.

1. WHAT IS THIS MEDICINE INTENDED FOR?

- as part of a combination therapy for controlled ovarian stimulation prior to in-vitro fertilisation.
- hormonal management of endometriosis (development of uterine mucosal cells outside of the uterus), including pain relief and reduction of endometrial lesions.
- treatment of uterine fibroids.

Therapeutic group:

gonadotrophin releasing hormone agonist.
This medicine works by reducing the normal response of your body to a hormone called gonadotrophin releasing hormone. As a result, your ovaries produce less of a hormone called oestrogen. After about one month of taking Synarel, this will cause your periods to either stop or be reduced in amount.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to gonadotrophin releasing hormone, its agonists, or any of the other ingredients in this medicine (see section 6).
- You are pregnant or may become pregnant whilst taking this medicine. If you are taking Synarel as part of a fertility programme, your pregnancy will be planned to take place after you stop taking this medicine.
- You suffer from vaginal bleeding that has not been diagnosed.
- You are currently breast-feeding.
- You are under 18 years of age.

Special warnings regarding use of the medicine

Before treatment with Synarel, tell your doctor if:

- You have "polycystic ovaries syndrome" as there is a potential risk for excessive ovarian stimulation.
- You think you might be pregnant, as there is a risk to the development of the foetus and/or of miscarriage.
- There have been reports of depression in patients taking Synarel which may be severe. If you are taking Synarel and develop depressed mood, inform your doctor.
- Use of Synarel in combination with gonadotropin to treat infertility can sometimes cause an overreaction in your ovaries (ovarian hyperstimulation syndrome, OHSS). You may notice stomach pain, swelling of your stomach, and feeling or being sick. If this happens, tell your doctor. See also section 4 'Side effects'.

Children and adolescents

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

Tests and follow-up

- After a first course of Synarel therapy, if further treatment of endometriosis and fibroids with Synarel is needed, your bone density may need to be checked.
- Tell your doctor if you are due to have any medical tests as use of this medicine might alter/affect the results.

Drug interactions

If you are taking or have recently taken, other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

- Nasal decongestants – Do not use these types of products within the 30 minute period before taking a dose of Synarel as they can significantly reduce absorption of the medicine in the nose. If your nose is congested, Synarel will still be absorbed properly.
- Oral contraceptives – If you have been using an oral contraceptive to prevent pregnancy, your doctor will ask you to stop taking these and use a barrier method of contraception (diaphragm, condom) to stop you becoming pregnant.

Using this medicine and food

You can take this medicine with or without food.

Pregnancy and breast-feeding

Do not take this medicine if you are pregnant or trying to become pregnant (see the section 'Do not use this medicine if:').
Do not take this medicine if you are breast-feeding.

Driving and using machines

Synarel is not known to affect the ability to drive or use machinery.

Important information about some of this medicine's ingredients

Synarel contains the substance benzalkonium chloride (a type of preservative). Benzalkonium chloride is an irritant and may cause skin reactions, swelling, and bronchial constriction.

3. HOW TO USE THIS MEDICINE?

Always use this preparation according to your doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.
The dosage and treatment regimen will be determined by your doctor only.

The standard dosage and duration are:

- When taken as part of a combination therapy for controlled ovarian stimulation prior to in-vitro fertilisation – one spray to one nostril in the morning, and one spray to the other nostril in the evening (2 sprays per day) or one spray to **each of**

the nostrils in the morning, and one spray to **each of the nostrils** in the evening (4 sprays per day), according to your doctor's instructions. Your doctor will specify your treatment duration. This will usually be for no longer than 12 weeks.

- Hormonal management of endometriosis (development of uterine mucosal cells outside of the uterus) – one spray to one nostril in the morning, and one spray to the other nostril in the evening (2 sprays per day). Your doctor may decide to increase your dose. You should use the spray for the first time between the second and fourth day of your period. Treatment duration is usually not longer than 6 months.
- Treatment of uterine fibroids – one spray to one nostril in the morning and one spray to the other nostril in the evening (2 sprays per day). Your doctor will specify your treatment duration. This will usually be for no longer than 3 months.

Do not exceed the recommended dose.

Taking this medicine: This medicine is for external use only – nasal solution (spray), do not swallow!
This medicine needs to reach your blood stream. If you swallow it, it breaks down in your digestive system and does not reach your blood stream.

If you sneeze while taking a spray of Synarel, take another dose of Synarel.

Directions for use – see directions for use below in this leaflet.

If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take this medicine at the scheduled time, take it as soon as you remember and take the next dose at your normal time. Do not take a double dose to make up for a forgotten dose.

If you miss one or more doses, vaginal bleeding may occur. Ovulation may also occur, so if you have had sexual intercourse and not used contraception while taking this treatment, there is a greater chance of pregnancy. It is then important that you stop taking Synarel and see your doctor to make sure that you are not pregnant (This is why it is very important to use a barrier method of contraception when you are taking this medicine).

Adhere to the treatment as recommended by your doctor. Even if your health improves, do not stop taking this medicine without consulting your doctor. If there is any medicine left after you have used 60 sprays, discard the remaining medicine.

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

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Synarel, may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Stop taking this medicine and tell your doctor straight away if you have an allergy to this medicine. You may experience this allergy as being short of breath, having chest pain, or a rash which may or may not be itchy.

Synarel may lead to enlargement of the ovaries due to excess egg production (OHSS – ovarian hyperstimulation syndrome). This can lead to pain in the pelvis, stomach or calf, swelling or feeling bloated, passing less urine, difficulty in breathing or an increase in weight. If you experience any of these symptoms, tell your doctor immediately.

Other side effects are listed below by frequency:

Very common side effects (affect more than one in 10 patients): weight increase, mood swings, sex drive decrease, headache, hot flushes, nasal irritation and/or inflammation, acne, oily skin and the formation of greasy scales, painful muscles, breast size decrease, vaginal dryness, oedema.

Common side effects (affect 1-10 in 100 patients): allergic reaction which may include shortness of breath, chest pain and a rash which may or may not be itchy, itching which may be accompanied by swelling, skin rash including hives, oestrogen deficiency, weight decrease, depression, tingling sensation, hypertension, hypotension, excessive hair growth, artificial menopause, abnormal bleeding from the vagina, sex drive increase, difficulty sleeping (insomnia), bone density decreases.

Uncommon side effects (affect 1-10 in 1,000 patients): hair loss, joint pain, breast size increase, ovarian cyst formation.

Side effects of unknown frequency (the frequency of these effects has not been established yet): migraine, blurred vision, palpitations, liver enzymes increase, short term increase in symptoms of endometriosis (development of uterine mucosal cells outside of the uterus), enlargement of the ovaries due to excess egg production (ovarian hyperstimulation syndrome, OHSS).

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link: <https://sideeffects.health.gov.il>

5. HOW TO STORE THE MEDICINE?

- You should always put the safety clip and the plastic dust cap back on when you are not using the medicine.
- Prevent poisoning! This and any other medicine should be kept 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 a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the bottle. The expiry date refers to the last day of that month.
- Store this medicine below 25°C, and protect from light and freezing.
- Use this product within 4 weeks of first opening.
- Keep the bottle upright.

6. FURTHER INFORMATION

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

sorbitol, glacial acetic acid, benzalkonium chloride, purified water and sodium hydroxide or hydrochloric acid to adjust the pH.
This medicine contains 71.4 mg/mL sorbitol.

What the medicine looks like and contents of the pack:

One metered spray bottle contains 8 mL of solution which supplies 60 doses (sprays).

Registration holder and address: Pfizer PFE Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725

Registration number of the medicine in the Ministry of Health's National Drug Registry: 135.64.26707

Revised in 06/2022 according to MOH guidelines

Directions for use

How to use Synarel® nasal solution

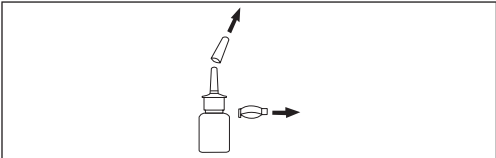
Important tips for using Synarel

- Your pump should produce a very fine spray (like mist), which can only happen by a quick and firm pumping action. It is normal to see some larger droplets of liquid within the fine mist. However, if Synarel comes out of the pump as a thin stream of liquid instead of a fine mist, Synarel may not work well, and you should consult your pharmacist.
- Be sure to clean the spray tip after priming the pump for first use. Clean the spray tip before and after every use, otherwise the spray tip can become clogged, which may result in you not getting the right amount of medicine that you were prescribed. Always replace the safety clip and the plastic dust cap after use to help prevent the spray tip becoming clogged.
- The pump is made to deliver a measured amount of medicine, no matter how hard you pump it.
- Do not try to make the tiny hole in the spray tip larger. If the hole is made larger the pump will spray a wrong dose of Synarel.

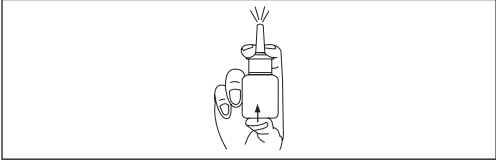
Priming the Spray Pump:

Before you use Synarel for the first time, you have to prime the spray pump. This only needs to be done once, before you take your first use.

1. Remove and save the safety clip and the plastic dust cap to uncover the nasal piece.
Hold the bottle in an upright position with two fingers on the 'shoulders' and your thumb on the bottom of the bottle.



2. Prime the pump by pressing the bottle upwards several times firmly and quickly until the air in the spray pump is expelled and a fine spray appears. This usually requires about 5 - 7 presses. It is not necessary to repeat this action during subsequent use. You will waste your medicine if you prime the pump every time you use it.



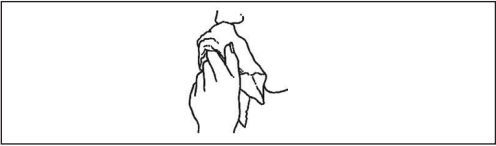
3. Clean the Spray Tip after Priming:
Hold the bottle in a horizontal position and rinse the spray tip with warm water, while wiping the tip with your finger or a clean soft cloth for 15 seconds.

Do not clean the spray tip with a pointed object. This could cause an improper dose of the spray to be delivered. Do not separate the pump from the bottle, as this will release the priming pressure.

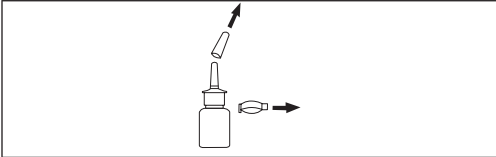
Wipe the tip dry with a clean soft and dry cloth or tissue.

Using the Spray Pump

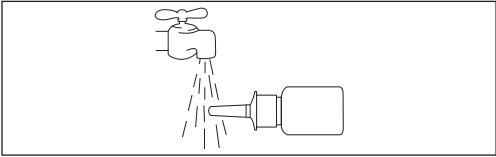
1. Gently blow your nose to clear the nostrils.



2. Remove and save the safety clip and the plastic dust cap to uncover the nasal piece. Hold the bottle as explained previously.



3. Clean the tip of the bottle. Hold the bottle in a horizontal position and rinse the spray tip with warm water, while wiping the tip with your finger or a clean soft cloth for 15 seconds.



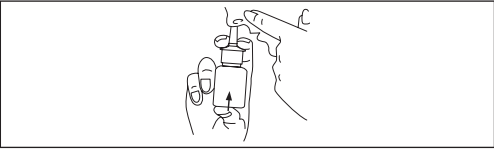
Do not clean the spray tip with a pointed object. This could cause an improper dose of the spray to be delivered. Do not separate the pump from the bottle, as this will release the priming pressure.

Wipe the tip dry with a clean soft and dry cloth or tissue.

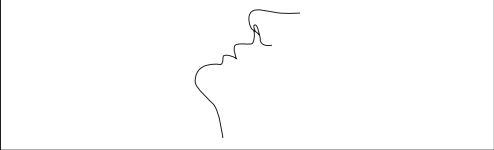
4. Bend your head forward slightly. Close one nostril and put the spray tip into the other, aiming towards the **back** and **outer side** of your nostril.



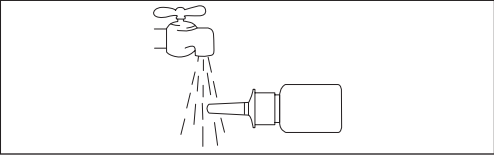
5. Press the bottle firmly between thumb and fingers **once only** whilst gently breathing in through the nostril. If your doctor has told you to take four doses every day, now repeat the action in your other nostril.



6. Remove the sprayer from the nose and bend your head backwards for a few seconds to let the spray spread in the back of the nose.



7. Clean the tip of the pump. Hold the bottle in a horizontal position and rinse the spray tip with warm water, while wiping the tip with your finger or a clean soft cloth for 15 seconds.



Do not clean the spray tip with a pointed object. This could cause an improper dose of the spray to be delivered. Do not separate the pump from the bottle, as this will release the priming pressure.

Wipe the tip dry with a clean soft cloth or tissue.
Cleaning the spray tip before and after use is important to prevent clogging of the tip that may cause you to get the wrong dose of medicine.

8. Replace the safety clip and the plastic dust cap. This is important, as it helps to prevent the spray tip becoming clogged.

