

**PATIENT PACKAGE INSERT IN
ACCORDANCE WITH THE PHARMACISTS'
REGULATIONS (PREPARATIONS) - 1986**
The medicine is dispensed with
a doctor's prescription only

Name of the preparation, its form and strength

Synarel® 2 mg/mL

Nasal Solution

Nafarelin acetate 2 mg/mL

Each actuation delivers: Nafarelin 200 mcg

A list of inactive and allergenic ingredients in the preparation is in section 6.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat 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.

The medicine is not intended for the treatment of young or adolescent girls under 18 years of age. **The medicine is intended for use in women only.**

For information on side effects, please refer to Section 4.

1. WHAT IS THE MEDICINE INTENDED FOR?

- As a part of combination treatment for supervised follicular stimulation, in preparation for in-vitro fertilization.
- Hormonal treatment of endometriosis (development of endometrial cells outside of the uterus).
- Treatment of uterine fibroids.

Therapeutic group:

Gonadotropin hormone agonist.

2. BEFORE USING THE MEDICINE

☒ Do not use the medicine if:

- x you are sensitive (allergic) to the active ingredient, to the gonadotropin hormone, to its agonists or to any of the other ingredients contained in the medicine, detailed in section 6.
- x you are pregnant or may become pregnant during treatment with the medicine. If you are taking Synarel® as part of fertility treatment, the pregnancy will be planned for after completion of the treatment period with this medicine.
- x you are breastfeeding.
- x you are suffering from undiagnosed vaginal bleeding.

Special warnings regarding use of the medicine

☒ Before treatment with Synarel®, tell the doctor if:

- you are suffering from polycystic ovaries, as there is a potential risk for excessive follicular stimulation.
- you think you might be pregnant, as there is a risk to the development of the fetus and/or of miscarriage.
- There have been reports of depression, that may be severe, in patients taking Synarel®. If you are taking Synarel® and develop a depressed mood, tell the doctor.

☒ If you are taking, or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist, especially if you are taking:

- nasal decongestants – do not use such preparations within the 30 minute period before using Synarel®, as they can significantly reduce the level of absorption of the medicine through the nose. If your nose is congested, Synarel® will still be absorbed properly.
- oral contraceptives – if you are taking oral contraceptives, your attending doctor will ask you to stop using them and to use a mechanical method of contraception instead (diaphragm, condom) to prevent pregnancy.

☒ Use of the medicine and food

Food has no effect on administration of the medicine.

☒ Pregnancy and breastfeeding

Do not use the medicine if you are pregnant or planning to become pregnant (see section: “Do not use the medicine if:”).

Do not use the medicine if you are breastfeeding.

☒ Driving and using machines

There is no evidence of an effect of the Synarel® preparation on the ability to drive or operate machines.

☒ Important information regarding some of the ingredients of the medicine

The Synarel® preparation contains benzalkonium chloride (a type of preservative). This substance is an irritant and may cause skin reactions, swelling and bronchospasm.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure.

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

Do not exceed the recommended dose.

Mode of administration: This medicine is intended for external use only – nasal solution (not for swallowing!)

Directions for use – see instructions for use further on in the leaflet.

Duration of treatment:

- As a part of combination treatment for supervised follicular stimulation, in preparation for in-vitro fertilization – duration of treatment will be determined by the doctor and will usually not exceed 8 weeks.
- Hormonal treatment of endometriosis (development of endometrial cells outside of the uterus) – duration of treatment will not exceed 6 months.
- Treatment of uterine fibroids – duration of treatment will not exceed 3 months.

If you took an overdose or if a child accidentally swallowed the medicine, immediately refer to a doctor or to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take this medicine at the designated time, take the dose as soon as you remember and the next dose as usual. Do not take a double dose to compensate for the forgotten dose.

If you missed one or more doses, vaginal bleeding may occur. In addition, ovulation may occur, and if you had sexual intercourse without adequate protection during the period of treatment, the risk of pregnancy increases. In this case, it is important to stop using Synarel® and refer to a doctor to make sure that you are not pregnant (therefore, it is very important to use mechanical methods of contraception when using this medicine).

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor. If some of the medicine remains, beyond the 60 actuations, discard it.

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

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

4. SIDE EFFECTS

As with any medicine, use of Synarel® may cause side effects in some patients. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Discontinue use and refer to a doctor immediately in the event of allergy to the preparation. The allergy may be manifested by shortness of breath, chest pain or rash, with or without itching.

Synarel® may lead to enlargement of the ovaries due to excess egg production (OHSS – Ovarian Hyperstimulation Syndrome). This condition can lead to pain in the pelvis, stomach or calf, swelling or bloated feeling, passing less urine, breathing difficulties or an increase in weight. If you experience one or more of these effects, refer to your doctor immediately.

Additional side effects are listed below according to their frequency:

Very common side effects (effects which occur in more than 1 in 10 patients):

weight increase, mood swings, decreased libido, headache, hot flushes, irritation and/or inflammation of the nasal mucosa, acne, seborrhea, muscle pain, reduction in breast size, vaginal dryness, edema.

Common side effects (effects which occur in 1-10 in 100 patients):

allergic reaction which may include shortness of breath, chest pain and a rash, with or without itching, itching which may be accompanied by swelling, skin rash including hives, estrogen deficiency, weight decrease, depression, tingling sensation, hypertension, hypotension, increased hair growth, artificial amenorrhea, abnormal vaginal bleeding, increased libido, insomnia, bone density decrease.

Uncommon side effects (effects that occur in 1-10 in 1,000 patients):

hair loss, joint pain, breast enlargement, ovarian cyst formation.

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

Migraine, blurred vision, palpitations, increase in liver enzymes, short term increase in symptoms of endometriosis (development of endometrial cells outside the uterus), enlargement of the ovaries due to excess egg production.

Tell your doctor if you are about to undergo medical tests, as treatment with the medicine may affect the results.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: <https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il>

5. HOW SHOULD THE MEDICINE BE STORED?

You should put the safety clip and the plastic cap back on the tip of the bottle whenever you are not using the medicine. Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach of children and/ or infants in order 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 bottle. The expiry date refers to the last day of that month.

Store below 25°C and protect from light and freezing.

After first opening: the preparation can be used for 4 weeks.

Keep the bottle upright.

6. FURTHER INFORMATION

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

Sorbitol, glacial acetic acid, benzalkonium chloride, purified water and sodium hydroxide or hydrochloric acid to adjust the pH.

The medicine contains 71.4 mg/mL sorbitol.

What the medicine looks like and the contents of the package:

A metered spray bottle containing 8 mL solution, which provides 60 doses (actuations).

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

Manufacturer and address: Pharmacia & Upjohn Co., Kalamazoo, USA.

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

This leaflet format has been determined by the Ministry of Health and the content thereof has been checked and approved in January 2018 and updated according to the guidelines of the Ministry of Health in October 2018

Synarel®

How to use Synarel® Nasal Solution

Important tips in regards to Synarel® use

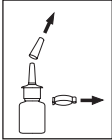
- The pump should produce a very fine mist (like fog), which can only be produced by pressing quickly and firmly. It is normal to see a few larger droplets of liquid within the fine mist. However, if Synarel® comes out of the pump as a thin stream of liquid instead of a fine mist, Synarel® may not work well, and you should consult the pharmacist.
- Be sure to clean the spray tip after priming the pump before first use. Clean the spray tip before and after every use, otherwise it may get clogged, which may lead to you not receiving the right amount of medicine prescribed for you. Always replace the safety clip and the plastic cap after use to help prevent the tip from becoming clogged.
- The pump is made to deliver a set amount of medicine, no matter how hard you press it.
- Do not try to enlarge the tiny hole in the spray tip. If the hole is enlarged, the pump will deliver a wrong amount of Synarel®.

Priming the pump for use

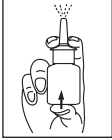
Before use of Synarel® for the first time, you must prime the pump. This only needs to be done once, before the first use.

1. Remove and save the safety clip and the plastic cap to expose the tip of the bottle.

Hold the bottle away from you, in an upright position, with two fingers resting 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 is expelled from the pump and a fine spray appears. This action usually requires about 5-7 presses. It is not necessary to repeat this action during subsequent uses. You will waste the medicine if you prime the pump this way each time you use it.



3. Clean the spray tip after priming it for use:

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

Do not clean the tip of the bottle with a sharp object, as it could cause an incorrect dosage to be sprayed. Do not separate the pump from the bottle, as this will release the initial pressure.

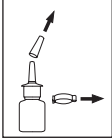
Wipe the tip with a soft, dry clean cloth or tissue paper.

Using the pump

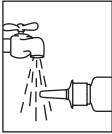
1. Gently blow your nose to clean the nostrils.



2. Remove and save the safety clip and the plastic cap to expose the tip of the bottle. Hold the bottle as described above.



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



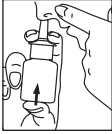
Do not clean the tip of the bottle with a sharp object, as it could cause an incorrect dosage to be sprayed. Do not separate the pump from the bottle, as this will release the initial pressure.

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

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



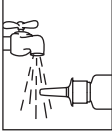
5. Press the bottle firmly between thumb and fingers **once only** while gently inhaling in through the nostril. If the doctor has instructed you to use four sprays every day, now repeat this action in the other nostril.



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



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



Do not clean the bottle tip with a sharp object, as this could cause an incorrect dosage to be sprayed. Do not remove the pump from the bottle, as this will release the priming pressure.

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

It is important to clean the tip before and after use to prevent it from getting clogged, which can lead to you receiving an incorrect dose of the medicine.

8. Put the safety clip and the plastic cap back in place. This is important in order to prevent the spray tip from getting clogged.

