

Package leaflet: Information for the user

Puregon® 900 IU/1.08 ml solution for injection follitropin beta

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Puregon is and what it is used for
2. What you need to know before you use Puregon
3. How to use Puregon
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1. What Puregon is and what it is used for

Puregon 900 IU/1.08 ml solution for injection contains follitropin beta, a hormone known as follicle-stimulating hormone (FSH).

FSH belongs to the group of gonadotrophins, which play an important role in human fertility and reproduction. In women, FSH is needed for the growth and development of follicles in the ovaries. Follicles are small round sacs that contain the egg cells. In men, FSH is needed for the production of sperm.

Puregon is used to treat infertility in any of the following situations:

Women

In women who do not ovulate and do not respond to treatment with clomifene citrate, Puregon can be used to cause ovulation.

In women undergoing assisted reproduction techniques, including *in vitro* fertilisation (IVF) and other methods, Puregon can bring about the development of multiple follicles.

Men

In men who are infertile due to lowered hormone levels, Puregon can be used for the production of sperm.

2. What you need to know before you use Puregon

Do not use Puregon

If you:

- are allergic to follitropin beta or any of the other ingredients of Puregon (listed in section 6)
- have a tumour of the ovary, breast, uterus, testis or brain (pituitary gland or hypothalamus)
- have heavy or irregular vaginal bleeding where the cause is unknown
- have ovaries that do not work because of a condition called primary ovarian failure

- have ovarian cysts or enlarged ovaries not caused by polycystic ovarian syndrome (PCOS)
- have malformations of the sexual organs which make a normal pregnancy impossible
- have fibroid tumours in the uterus which make a normal pregnancy impossible
- are a man and are infertile because of a condition called primary testicular failure.

Warnings and precautions

Talk to your doctor before using Puregon if you:

- have had an allergic reaction to certain antibiotics (neomycin and/or streptomycin)
- have uncontrolled pituitary gland or hypothalamic problems
- have an underactive thyroid gland (hypothyroidism)
- have adrenal glands that are not working properly (adrenocortical insufficiency)
- have high prolactin levels in the blood (hyperprolactinemia)
- have any other medical conditions (for example, diabetes, heart disease, or any other long-term disease).

If you are a woman:

Ovarian hyperstimulation syndrome (OHSS)

Your doctor will check the effects of the treatment regularly to be able to choose the correct dose of Puregon from day to day. You may regularly have ultrasound scans of the ovaries. Your doctor may also check blood hormone levels. This is very important since too high a dose of FSH may lead to rare but serious complications in which the ovaries are overly stimulated and the growing follicles become larger than normal. This serious medical condition is called ovarian hyperstimulation syndrome (OHSS). In rare cases, severe OHSS may be life-threatening. OHSS causes fluid to build up suddenly in your stomach and chest areas and can cause blood clots to form. Call your doctor right away if you notice severe abdominal swelling, pain in the stomach area (abdomen), feeling sick (nausea), vomiting, sudden weight gain due to fluid buildup, diarrhoea, decreased urine output or trouble breathing (see also section 4 on Possible side effects).

→ Regular monitoring of the response to FSH-treatment helps to prevent ovarian overstimulation.

Contact your doctor immediately if you are experiencing stomach pains, also if this occurs some days after the last injection has been given.

Multiple Pregnancy or birth defects

After treatment with gonadotrophin preparations, there is an increased chance of having multiple pregnancies, even when only one embryo is transferred into the uterus. Multiple pregnancies carry an increased health risk for both the mother and her babies around the time of birth. Furthermore, multiple pregnancies and characteristics of the patients undergoing fertility treatment (e.g. age of the female, sperm characteristics, genetic background of both parents) may be associated with an increased risk of birth defects.

Pregnancy complications

There is a slightly increased risk of a pregnancy outside the uterus (an ectopic pregnancy). Therefore, your doctor should perform an early ultrasound examination to exclude the possibility of pregnancy outside the uterus.

In women undergoing fertility treatment there may be a slightly higher chance of a miscarriage.

Blood clot (Thrombosis)

Treatment with Puregon, just as pregnancy itself, may increase the risk of having a blood clot (thrombosis). Thrombosis is the formation of a blood clot in a blood vessel.

Blood clots can lead to serious medical conditions, such as:

- blockage in your lungs (pulmonary embolus)
- stroke

- heart attack
- blood vessel problems (thrombophlebitis)
- a lack of blood flow (deep venous thrombosis) that may result in a loss of your arm or leg.

Please discuss this with your doctor, before starting treatment, especially:

- if you already know you have an increased chance of having thrombosis
- if you, or anyone in your immediate family, have ever had a thrombosis
- if you are severely overweight.

Ovarian torsion

Ovarian torsion has occurred after treatment with gonadotropins including Puregon. Ovarian torsion is the twisting of an ovary. Twisting of the ovary could cause the blood flow to the ovary to be cut off.

Before starting to use this medicine, tell your doctor if you:

- have ever had ovarian hyperstimulation syndrome OHSS
- are pregnant or think that you may be pregnant
- have ever had stomach (abdominal) surgery
- have ever had a twisting of an ovary
- have past or current cysts in your ovary or ovaries.

Ovarian and Other Reproductive System Tumours

There have been reports of ovarian and other reproductive system tumors in women who have had infertility treatment. It is not known if treatment with fertility medicines increases the risk of these tumors in infertile women.

Other medical conditions

In addition, before starting to use this medicine, tell your doctor if you:

- have been told by a doctor that pregnancy would be dangerous for you.

If you are a man:

Men with too much FSH in their blood

Increased FSH blood levels are a sign of damage to the testicles. Puregon is usually not effective in such cases. To check the effects of treatment, your doctor may ask you for a semen sample to be analysed, four to six months after the start of treatment.

Other medicines and Puregon

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

If Puregon is used in a combination with clomifene citrate, the effect of Puregon may be increased. If a GnRH agonist (a medicine used to prevent early ovulation) has been given, higher doses of Puregon may be needed.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine. You should not use Puregon if you are already pregnant, or think you might be pregnant.

Puregon may affect milk production. It is unlikely that Puregon is passed into breast milk. If you are breast-feeding, tell your doctor before using Puregon.

Driving and using machines

Puregon is unlikely to affect your ability to drive or use machines.

Important information about some of the ingredients of Puregon

This medicinal product contains less than 1 mmol sodium (23 mg) per injection, i.e. essentially 'sodium-free'.

Children

There is no relevant use of PUREGON in children.

3. How to use Puregon

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Dosage in women

Your doctor will decide on your starting dose. This dose may be adjusted during your treatment period. Further details on the treatment schedule are given below.

There are large differences between women in the response of the ovaries to FSH, which makes it impossible to set a dosage schedule which is suitable for all patients. To find the right dosage, your doctor will check your follicle growth by means of ultrasound scanning, and measurement of the amount of oestradiol (female sex hormone) in the blood.

* *Women who are not ovulating*

A starting dose is set by your doctor. This dose is continued for at least seven days. If there is no ovarian response, the daily dose will then be gradually increased until follicle growth and/or plasma oestradiol levels indicate a proper response. The daily dose is then maintained until a follicle of proper size is present. Usually, 7 to 14 days of treatment are sufficient. Puregon treatment is then stopped and ovulation will be induced by giving human chorionic gonadotrophin (hCG).

* *Medically assisted reproduction programs, for instance IVF*

A starting dose is set by your doctor. This dose is continued for at least the first four days. After this, your dose may be adjusted, based upon your ovarian response. When a sufficient number of follicles of proper size are present, the final phase of maturation of the follicles is induced by giving hCG. Retrieval of the egg(s) is performed 34-35 hours later.

Dosage in men

Puregon is usually prescribed at a dose of 450 IU per week, mostly in 3 dosages of 150 IU, in combination with another hormone (hCG), for at least 3 to 4 months. The treatment period equals the development time of sperm and the time in which improvement can be expected. If your sperm production has not started after this period, your treatment may carry on for at least 18 months.

How are the injections given

Puregon solution for injection in cartridges has been developed for use in the Puregon Pen. The separate instructions for using the pen must be followed carefully. Do not use the cartridge if the solution contains particles or if the solution is not clear.

Using the pen, injections just under the skin (in the lower stomach, for example) can be given by yourself or your partner. Your doctor will tell you when and how to do this. If you inject yourself with Puregon, follow the instructions carefully to give Puregon properly and with minimal discomfort. The very first injection of Puregon should only be given in the presence of a doctor or nurse.

If you use more Puregon than you should

Tell your doctor immediately.

Too high a dose of Puregon may cause hyperstimulation of the ovaries (OHSS). This may be noticed as pain in the stomach. If you are troubled by stomach pains, tell your doctor immediately. See also section 4 on possible side effects.

If you forget to use Puregon

If you forget a dose do not use a double dose to make up for a missed dose.

→ Contact your doctor.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects in women

A complication with FSH treatment is hyperstimulation of the ovaries. Ovarian overstimulation may develop into a medical condition called **ovarian hyperstimulation syndrome (OHSS)**, which can be a serious medical problem. The risk can be reduced by careful monitoring of follicular development during treatment. Your doctor will do ultrasound scans of your ovaries to carefully monitor the number of maturing follicles. Your doctor may also check blood hormone levels. Pain in the stomach, feeling sick or diarrhoea are the first symptoms. In more severe cases symptoms may include enlargement of the ovaries, accumulation of fluid in the abdomen and/or chest (which may cause sudden weight gain due to fluid buildup) and the occurrence of blood clots in the circulation. See warnings and precautions in section 2.

→ Contact your doctor immediately if you are experiencing stomach pains, or any of the other symptoms of ovarian hyperstimulation, also if this occurs some days after the last injection.

If you are a woman:

Common side effects (may affect up to 1 in 10 people):

- Headache
- Injection site reactions (such as bruising, pain, redness, swelling and itching)
- Ovarian hyperstimulation syndrome (OHSS)
- Pelvic pain
- Stomach pain and/or bloating

Uncommon side effects (may affect up to 1 in 100 people):

- Breast complaints (including tenderness)
- Diarrhoea, constipation or stomach discomfort
- Enlargement of the uterus
- Feeling sick
- Hypersensitivity reactions (such as rash, redness, hives and itching)
- Ovarian cysts or enlargement of the ovaries
- Ovarian torsion (twisting of the ovaries)
- Vaginal bleeding

Rare side effects (may affect up to 1 in 1,000 people):

- Blood clots (this may also occur in the absence of unwanted overstimulation of the ovaries, see warnings and precautions in section 2)

Pregnancy outside the uterus (an ectopic pregnancy), miscarriage and multiple pregnancies have also been reported. These side effects are not considered to be related to the use of Puregon, but to Assisted Reproductive Technology (ART) or subsequent pregnancy.

If you are a man:

Common side effects (may affect up to 1 in 10 people):

- Acne
- Injection site reactions (such as hardening and pain)
- Headache
- Rash
- Some breast development
- Testicular cyst

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects, you can help provide more information on the safety of this medicine.

United Kingdom: Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

Ireland: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie

Malta: ADR Reporting at: www.medicinesauthority.gov.mt/adrportal

5. How to store Puregon

Keep this medicine out of the sight and reach of children.

Storage by the pharmacist

Store at 2°C – 8°C (in a refrigerator). Do not freeze.

Storage by the patient

You have two options:

1. Store at 2°C – 8°C (in a refrigerator). Do not freeze.
 2. Store at or below 25 °C (at room temperature) for a single period of not more than 3 months.
- Make a note of when you start storing the product out of the refrigerator.

Keep the cartridge in the outer carton.

Once the rubber inlay of a cartridge is pierced by a needle, the product may be stored for a maximum of 28 days.

Please put the day of first use of the cartridge on the dosing record table as shown in the Instruction Manual of the Puregon Pen.

Do not use Puregon after the expiry date which is stated on the label and carton after 'EXP'. The expiry date refers to the last day of that month.

Discard used needles immediately after injection.

Do not mix any other drug into the cartridges.

Empty cartridges must not be refilled.

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. Contents of the pack and other information

What Puregon contains

- Each cartridge contains the active substance follitropin beta, a hormone known as follicle-stimulating hormone (FSH) in a strength of 833 IU/ml aqueous solution.
- The other ingredients are sucrose, sodium citrate, L-methionine, polysorbate 20 and benzyl alcohol in water for injections. The pH may have been adjusted with sodium hydroxide and/or hydrochloric acid.

What Puregon looks like and contents of the pack

Puregon solution for injection (injection) is a clear, colourless liquid. It is supplied in a glass cartridge. It is available in packs of 1 cartridge.

Marketing Authorisation Holder

Merck Sharp & Dohme Limited, Hertford Road, Hoddesdon, Hertfordshire EN11 9BU, United Kingdom

Manufacturer

N.V. Organon, Kloosterstraat 6, 5349 AB Oss, The Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in February 2014.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>.

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