PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrPUREGON®

Follitropin Beta

Read this carefully before you start taking **PUREGON** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **PUREGON**.

What is PUREGON used for?

The name of your medicine is PUREGON. It contains follicle-stimulating hormone (FSH) in a solution in a cartridge. PUREGON is produced by mammalian cells, which by recombinant DNA technology were changed to carry the genes for human FSH.

PUREGON belongs to a group of medicines called "gonadotropins".

- In women, FSH is important for the monthly ripening of the follicle, a tiny cyst in the ovary in which the egg cell develops. If the body does not produce enough FSH, infertility may be the result. In these cases PUREGON can be used to make up for the shortage. To determine the right dosage, a daily check may be necessary. Follicle ripening is determined by means of ultrasound, and the amount of estrogens (female hormones) in blood can be measured. When the follicle is big enough, a hormone preparation with a strong LH activity is given (human chorionic gonadotropin, hCG). This causes ovulation (release of the egg).

In spite of careful monitoring, often more than one egg cell is released. This increases the chance of having more than one baby.

Poor production of FSH is not the only reason for infertility. In these cases medically assisted reproduction programs can sometimes be used, for instance in vitro ("test tube") fertilization. For this technique several egg cells are needed and PUREGON can then be used to cause a number of egg cells to develop.

- In men, it is used to increase the production of sperm in those who have a deficiency due to hypogonadotrophic hypogonadism.

How does PUREGON work?

PUREGON is very similar to the natural human FSH, which is normally secreted by a small gland at the base of the brain, the pituitary. Together with luteinizing hormone (LH), FSH controls the action of the sexual glands (ovaries in women and testes in men).

What are the ingredients in PUREGON?

Medicinal ingredient: follitropin beta

Non-medicinal ingredients: benzyl alcohol, L-methionine, polysorbate 20, sodium citrate, sucrose, water for injection.

PUREGON comes in the following dosage forms:

PUREGON is presented as a sterile solution in cartridges in strength of 833 IU/mL. The 300 IU/0.36 mL cartridge contains 0. 480 mL for a net total deliverable dose of 300 IU, the 600 IU/0.72 mL cartridge contains 0.840 mL for a net total deliverable dose of 600 IU and the 900 IU/1.08 mL cartridge contains 1.23 mL for a net total deliverable dose of 900 IU.

Do not use PUREGON if:

- You have a high circulating FSH level indicating primary ovarian failure or primary testicular failure.
- You have uncontrolled thyroid or adrenal dysfunction.
- You have a tumour of the ovary, breast, uterus, testis or brain (hypothalamus or pituitary gland).
- You are pregnant or think you may be pregnant.
- You are breast-feeding.
- You have heavy or irregular vaginal bleeding of undetermined origin.
- You have an ovarian cyst or enlargement not due to polycystic syndrome (PCOS).
- You are allergic (hypersensitive) to follitropin beta or any of the other ingredients of PUREGON.
- You have conditions incompatible with pregnancy such as malformations of reproductive organs or fibroid tumours of the uterus.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take PUREGON. Talk about any health conditions or problems you may have, including if you:

- Have experienced an allergic reaction to neomycin and/or streptomycin (antibiotics) in the past.
- 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 and
    - Have ever had ovarian hyperstimulation syndrome OHSS.
    - Have ever had stomach (abdominal) surgery.
    - Have ever had a twisting of an ovary.
    - Have past or current cysts in your ovary or ovaries.

Other warnings you should know about:

Blood Clots

Treatment with gonadotropins may increase the risk of having a blood clot (thrombosis). Thrombosis is the formation of a blood clot in your veins or arteries. Please tell your doctor prior to starting treatment, if you already know you have an increased risk for thrombosis, if you or anyone in your immediate family has ever had a thrombosis, or if you are severely overweight. It should be noted, however, that pregnancy itself also carries an increased risk of thrombosis.

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.

Ovarian Hyperstimulation Syndrome

Close supervision of patients by a doctor is very important. Usually ultrasound scans of the ovaries are performed. Your doctor may also check blood hormone levels. The results of these tests allow the doctor to choose the proper dose from day to day. This is very important since too high a dose 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.

The risk can be reduced by careful monitoring of follicle development during treatment. Your doctor will do ultrasound scans of your ovaries to carefully monitor the number of maturing follicles. The first symptoms of ovarian overstimulation may be noticed as pain in the stomach (abdomen), feeling sick or diarrhea. 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.

Contact your doctor without delay if you are experiencing any of these symptoms, also if they develop some days after the last injection has been given.

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.

Previous Diseases

Women with risk factors for thrombosis (previous episode of thrombosis, family history of thrombosis or a genetic condition that predisposes her to thrombosis) may have an increased risk of a venous or arterial thromboembolic event upon treatment with gonadotropins.

Reproductive Issues

After treatment with gonadotropin 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. There are also potential risks associated with multiple births including a higher rate of spontaneous abortion.

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

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

Other Medical Conditions

Before starting to use this medicine, tell your doctor if you have been told by a doctor that pregnancy would be dangerous for you.

Pregnancy

In pregnancies occurring after treatment with gonadotropic preparations, there is an increased risk of having twins or multiple births.

There is a slightly increased risk of a pregnancy outside of the uterus (an ectopic pregnancy). Early ultrasound confirmation that a pregnancy is intra-uterine is therefore important.

If you are a man

Elevated FSH blood levels are indicative of testicular damage. PUREGON is usually not effective in such cases. To monitor treatment, your doctor may ask for a semen analysis to be performed 4 to 6 months after the beginning of treatment.

Ability to drive or operate machinery

As far as is known, PUREGON has no effect on alertness and concentration.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with PUREGON:

- Clomiphene

How to take PUREGON:

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.

Usual dose:

For Females:

Your doctor will decide on the dose of PUREGON to be given. This dose may be increased as your treatment progresses.

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

For Males:

PUREGON is usually prescribed at a dose of 450 IU per week, mostly given in 3 dosages of 150 IU per week **or** (also considered acceptable two dosages of 225 IU per week) both regimens given in combination with another hormone (hCG), for at least 3 to 4 months. Semen analysis is recommended 4 to 6 months after start of treatment to assess the response. If you have not responded after this period, your treatment may continue up to 48 weeks. Current clinical experience with other gonadotropins suggests that treatment for up to 18 months or longer may be necessary to achieve spermatogenesis.

How the Injections are Given:

Using the pen, the injections are given slowly under the skin (for instance in the abdominal wall or in the upper thigh). The needle should be inserted at a 90^{o} angle to the surface of the skin.

To prevent painful injections and minimise leakage from the injection site, PUREGON should be slowly administered subcutaneously.

By whom: Using the solution in cartridges with the PUREGON PEN, injections just under the skin can be given by you or your partner. Your doctor will tell you when and how to do this. The first injection of PUREGON should be given under medical supervision.

For women, the PUREGON solution for injection can be injected under the skin or into a muscle. Injections just under the skin can be given by you or your partner. The injections into a muscle should only be given by a doctor or nurse. For men, the PUREGON solution for injection can only be administered under the skin since injection into a muscle has not been investigated in this population. Your doctor will tell you when and how to inject. The first injection of PUREGON should be given under medical supervision.

Overdose:

The acute toxicity of gonadotropins has been shown to be very low. Too high a dosage for more than one day may lead to hyperstimulation of the ovaries (OHSS).

If you think you, or a person you are caring for, have taken too much PUREGON, contact a healthcare professional, hospital emergency department, or regional poison control centre

immediately, even if there are no symptoms.

Missed Dose:
If you miss a dose contact your doctor. Do not double the next dose.

What are possible side effects from using PUREGON?

These are not all the possible side effects you may feel when taking PUREGON. If you experience any side effects not listed here, contact your healthcare professional.

Side Effects in Females:

- vaginitis
- stomach pain and / or bloating
- nausea, diarrhea, constipation or stomach discomfort
- urinary tract infection
- ovarian cysts or enlargement of the ovaries
- headache
- vomiting
- laboured breathing, nasal congestion, sore throat, upper respiratory tract infection
- nervousness
- reactions at the site of injection: bruising, pain, redness, swelling and itching
- hypersensitivity reactions including, rash, redness, hives and itching
- pelvic pain
- breast complaints (including tenderness)
- enlargement of the uterus
- feeling sick
- vaginal bleeding
- hemoperitoneum

Side Effects in Males:

- acne
- hardening of the injection site
- headache
- rash
- some breast development
- testicular cyst

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.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
COMMON			
Ovarian hyperstimulation syndrome (OHSS): pain in your lower abdomen area, nausea, vomiting, weight gain, diarrhea, decreased urine output, trouble breathing		√	
UNCOMMON			
Ovarian torsion (twisting of the ovaries): abdominal pain, nausea			√
RARE			
Blood clots: blood vessel problems (thrombophlebitis), swelling and pain in arm or leg, stroke, heart attack, difficulty breathing or chest pain, loss of your arm or leg, blood clot in your lungs (pulmonary embolus), heart attack			√
UNKNOWN			
Sudden, severe allergic reactions: breathing difficulty, swelling, hives, lightheadedness, fast heartbeat, sweating and loss of consciousness			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Keep out of reach and sight of children. Do not use past expiry date. Protect from light.

Do not use if the solution contains particles or if the solution is not clear.

Patient: Store in a refrigerator (2°C - 8°C). Do not freeze or store at or below 25°C for a maximum of 3 months (keep the cartridges in the outer carton).

PUREGON Solution for Injection in Cartridge:

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

If you want more information about PUREGON:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.organon.ca, or by calling 1-844-820-5468.

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