

GONAL-F[®] POWDER AND SOLVENT FOR SOLUTION FOR INJECTION

Follitropin alfa (450 IU/0.75 ml, 75 IU/ml)

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What Gonal-F is used for

Gonal-F can be used to bring about the development of follicles (each follicle contains one egg) in women who are not ovulating and who have not responded to treatment with clomiphene citrate.

Gonal-F is also used to stimulate the development of several follicles in women undergoing assisted reproductive technologies (ART) such as in vitro fertilization (IVF).

How Gonal-F works

Gonal-F contains follitropin alfa, which is similar to follicle stimulating hormone (FSH) found naturally in humans.

Gonal-F belongs to a class of hormones called gonadotrophins. FSH is necessary for the growth and development of egg cells (follicles) in women.

Before you use Gonal-F

- *When you must not use it*

Do not use Gonal-F if you have a history of allergy to any of the ingredients listed at the end of this leaflet.

Do not use Gonal-F if you have tumours of the hypothalamus or pituitary gland (both are part of the brain).

Do not use Gonal-F if you:

- are pregnant
- are breastfeeding
- have enlarged ovaries
- have an unexplained ovarian cyst

- have unexplained vaginal or uterine bleeding
- have cancer of the ovaries, uterus or breasts
- ovaries have failed
- have fibroids in your uterus or malformations of sexual organs which would make pregnancy impossible
- have testicular insufficiency

- *Before you start to use it*

Your doctor will assess you and your partner's fertility. This may include tests for other medical conditions, which may interfere with your ability to become pregnant. If necessary, other medical conditions may be treated before starting infertility treatments including Gonal-F.

Tell your doctor if you have any allergies to any foods, dyes, preservatives or any other medicines. Tell your doctor if you have or have had any of the following medical conditions:

- disorders of the thyroid gland
- disorders of the adrenal glands
- high prolactin levels in the blood
- porphyria or a family history of porphyria (inability to breakdown porphyrin that can be inherited)

Your doctor will assess if you have any medical conditions which interfere with your ability to become pregnant.

Ovarian Hyperstimulation Syndrome (OHSS)

Treatment with Gonal-F may increase your risk of developing a condition called ovarian hyperstimulation syndrome (OHSS). This is when the ovaries over-react to the hormonal treatment and become larger.

The most common symptom is lower abdominal pain. During stimulation your doctor will monitor your treatment by the use of ultrasound and/or blood tests to help determine if

you are likely to develop OHSS. If necessary your doctor will delay or cancel your Gonal-F injection. You may also be advised to refrain from sexual intercourse until the end of the cycle if this occurs.

Multiple Pregnancies

Compared to natural conception, the frequency of multiple pregnancies and births is higher in people receiving treatments that stimulate follicle growth for ovulation induction. The majority of these are twins. Your doctor will monitor your response to treatment to minimize the chance of multiple pregnancies, because of the greater risks they carry for mothers and babies.

Miscarriage / Abortion

Compared to natural conception, the frequency of pregnancy loss is higher in people undergoing treatments to stimulate follicle growth for ovulation induction.

Birth Defects

There may be a slight increased risk of birth defects in women using assisted reproductive technologies. This may be due to differences in maternal age, sperm characteristics or multiple pregnancies.

Blood Clot Disorders

Tell your doctor if you or a family member have or have had signs of blood clots (e.g. pain, warmth, redness, numbness or tingling in the arm or leg).

Treatment with Gonal-F and hCG may increase the risk of blood clots forming in your blood vessels. Talk to your doctor about any concerns you may have before undergoing treatment or before you start using Gonal-F.

- *Taking other medicines*

Tell your doctor if you are taking any other medicines, including:

- all prescription medicines

- any medicines, vitamins, herbal supplements or natural therapies you buy without prescription from your pharmacy, supermarket, naturopath or health food shop
- Some medicines may be affected by Gonal-F or may affect how well it works. Your doctor has more information on medicines to be careful with or avoid while using Gonal-F.

How to use Gonal-F

Follow all directions given to you by your doctor, nurse or pharmacist carefully.

They may differ from the information contained in this leaflet.

Treatment with Gonal-F should be started under the supervision of a specialist doctor experienced in fertility treatment.

Gonal-F is given as a course of daily injections.

You should have your injection at the same time each day.

- How much to use

Your doctor will decide the correct dose of Gonal-F for you. Your dose of Gonal-F may be adjusted depending on your individual response to treatment. Please consult your doctor if you are in any doubt.

The following is a guide to the common dose.

1. *Women who are not ovulating*

The common dose usually starts at 75-150IU (5.46-10.92 microgram) daily, commencing within the first 7 days of the menstrual cycle. The dose may be adjusted as your treatment progresses. The maximal daily dose is usually not higher than 225 IU (16.5 microgram). If a person fails to respond adequately after 4 weeks of treatment, that cycle should be abandoned and she may recommence treatment at a higher starting dose than in the abandoned cycle.

2. *Women undergoing assisted reproductive technologies*

The common dose usually starts at 150-225 IU (10.92-16.38 microgram) daily, commencing on day 2 or 3 of the cycle. The dose may be adjusted as your treatment progresses. The maximal daily dose is usually not higher than 450 IU (32.76 microgram). In general, adequate

follicular development is achieved on average by the tenth day of treatment (range 5 to 20).

- How to inject

Gonal-F is given as a subcutaneous (under your skin) injection in the lower abdominal area or thigh. The first injection of Gonal - F should be performed under direct medical supervision.

This is a multidose medicine intended for several injections.

Gonal-F is intended to be injected by you or your partner.

Alternatively your doctor or a nurse may give you these injections.

If your doctor or nurse decides you can give the injections yourself, the doctor or nurse will teach you the injection technique.

Do not self-inject until you are sure of how to do it.

Read the Instructions for Use provided in the pack carefully before commencing injections.

Your partner may be trained to give the injection at home.

- Where to inject

Gonal-F is usually given in the lower abdominal area (except around the navel and waistline) or the front of your thigh. The injection site should be changed daily to lessen possible injection site reactions.

Do not inject into any areas in which you feel lumps, firm knots, depressions, pain, or see any discolouration.

Talk to your doctor if you find anything unusual when injecting.

- When to use it

Your doctor will decide how much medicine you will take and how often.

- How long to use it

The length of treatment varies with each individual. It is possible to have more than one treatment cycle of Gonal-F.

- If you forget to use it

If you forget an injection or are not sure what to do, contact your doctor or nurse immediately for advice. Do not inject a double dose on any day.

Ask your doctor if you are not sure what to do or have trouble

remembering to inject your medicine.

- If you use too much (overdose)

Immediately contact your doctor if you are concerned that you have given yourself too much or someone else has injected themselves with Gonal-F. Nevertheless, there is a possibility that ovarian hyperstimulation syndrome (OHSS) may occur.

While you are using Gonal-F

- Things you must do

See your doctor regularly.

Your doctor will monitor you closely throughout your treatment.

If you are about to be started on any new medicine, tell your doctor and pharmacist that you are using Gonal-F.

If you plan to have surgery, tell your doctor or dentist that you are using Gonal-F.

Tell all doctors, dentists and pharmacists who are treating you that you are using Gonal-F.

Tell your doctor immediately if you become pregnant while using Gonal-F.

- Things you must not do

If you are self-injecting do not:

- Stop using Gonal-F without telling your doctor.
- Change the dose unless your doctor tells you to. Changing your dose without advising your doctor can increase your risk of unwanted side effects or can prevent the medicine from working properly.
- Give this medicine to anyone else, even if their symptoms seem similar to yours or if they have the same condition as you.

- Things to be careful of

Be careful driving or operating machinery until you know how Gonal-F affects you.

Side effects

Tell your doctor as soon as possible if you do not feel well while using Gonal-F.

All medicines can have side effects. Sometimes they are serious, most of the time they are not.

Do not be alarmed by this list of possible side effects.

You may not experience any of them.

Ask your doctor or pharmacist to answer any questions you may have.

If you get any side effects, do not stop using Gonal-F without first talking to your doctor.

Tell your doctor immediately, or go to Accident and Emergency at your nearest hospital if you notice any of the following:

- signs of an allergic reaction, including swelling of the face, lips, tongue, or other parts of the body; shortness of breath, wheezing or difficulty breathing;
- severe skin rash, itching or hives.

Tell your doctor if you notice any of the following and they worry you:

- pain, redness, irritation or swelling at the site of injection during your treatment with Gonal-F
- signs of severe ovarian hyperstimulation syndrome (OHSS) such as severe lower abdominal pain, severe pelvic pain, nausea, vomiting, diarrhoea followed by rapid weight gain, reduced amounts of urine and shortness of breath
- warning signs of stroke or heart attack
- warning signs of blood clots such as pain, warmth, redness in your arm or leg
- ectopic pregnancy (embryo implanted outside the womb) may occur, especially in women with prior tubal disease.
- headache, dizziness
- stomach pain, abdominal distension or abdominal discomfort

Other side effects not listed above may also occur in some people.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-78835550, or visiting the website npra.moh.gov.my (Public → Reporting Medicinal Problems / Side Effects / AEFI / Vaccine Safety).

Storage and Disposal of Gonal-F

- Storage

Do not freeze. The reconstituted solution is stable for 28 days, do not store above 25°C.

Store in the original package, in order to protect from light.

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

Do not use the product after the expiry date printed on the label.

Do not use Gonal-F if you notice any visible signs of deterioration or damage to the container. Keep this medicine where children cannot reach it.

- Disposal

If you are self-injecting, you should discard all sharps into a disposal unit. If you have any Gonal-F that has expired or is left over from your treatment refer this to your clinic.

Product description

- What it looks like

Gonal-F 450 IU/0.75 ml

GONAL-F is presented as a powder and colourless, transparent solvent for injection. The powder is presented in 3 ml vials (Type I glass), with rubber stopper (bromobutyl rubber) and aluminium seal ring and colour flip off cap. The solvent for reconstitution is presented in 1 ml pre-filled syringes (Type I glass) with a rubber stopper. The administration syringes made of polypropylene with a stainless steel pre-fixed needle are also provided. The medicinal product is supplied as a pack of 1 vial of powder with 1 pre-filled syringe of solvent for reconstitution and 6 disposable syringes for administration graduated in FSH units

Gonal-F 75 IU/ml

GONAL-F is presented as a powder and solvent for injection. The powder is presented in 3 ml vials (Type I glass), with rubber stopper (bromobutyl rubber) and aluminium flip-off cap. The 1 ml solvent for reconstitution is presented in either 2 or 3 ml vials (Type I glass) with rubber stopper (tefloncoated rubber) or in 1 ml pre-filled syringes (Type I glass) with a rubber stopper. The medicinal product is supplied in packs of 1 vial of powder with 1 vial of solvent, or packs of 1, 5, or 10 vials of powder with 1, 5 or 10 of solvent pre-filled syringe. Not all pack sizes may be marketed.

- Ingredients:

- Active ingredient: Follitropin alfa

- Inactive ingredients:

Gonal-F 450 IU/0.75 ml

Sucrose, sodium dihydrogen phosphate monohydrate, Disodium phosphate dihydrate, Phosphoric acid, Concentrated Sodium hydroxide, Water for injection

Gonal-F 75 IU/ml

Sucrose, Sodium dihydrogen phosphate monohydrate, Disodium phosphate dihydrate, Methionine, Polysorbate 20, Phosphoric acid, Concentrated Sodium hydroxide

- MAL Number:

GONAL-F® 450 IU/0.75ml:
MAL20112175AZ

GONAL-F® 75 IU/ml:
MAL20112177AZ

Manufacturer

Gonal-F 450 IU/0.75 ml

Merck Serono S.p.A, Via delle Magnolie 15 (Zona Industriale), I-70026, Bari Italy

Gonal-F 75 IU/ml

Merck Serono S.A.
Succursale d'Aubonne,
Zone industrielle de l'Ouriettaz,
1170 Aubonne, Switzerland.

Product Registration Holder

Merck Sdn Bhd (178145-V)
Level 3, Menara Sunway Annexe,
Jalan Lagoon Timur
Bandar Sunway
46150, Petaling Jaya
Selangor Darul Ehsan

Date of Revision:

20/06/2017

Serial Number:

BPFK(R4/1)150617/00131

How to prepare and use the powder and solvent Gonal-F

- This section tells you how to prepare and use your GONAL-F powder and solvent.
- Before starting the medicine, please read all the instructions carefully.
- Inject the medicine at the same time every day.

1. Wash your hands and find a clean place.

- You should keep your hands and items you use as clean as possible.
- The ideal place is a desk or a clean kitchen surface

2. Take all the items you need and put it on the table:

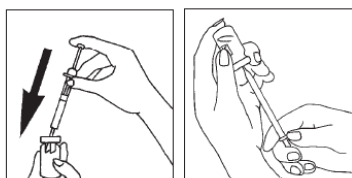
- 1 pre-filled syringe of solvent (the clear liquid)
- 1 vial containing GONAL-F (the white powder)
- 1 needle for preparation
- 1 fine bore needle for injection subcutaneously

Not included in the pack:

- 2 alcohol swab
- 1 sharp container

3. Preparation of solution:

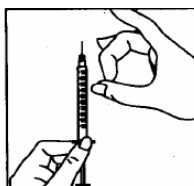
- Remove the protective cap from the powder vial and syringe filled with solvent.
- Attach the needle for preparation on solvent filled syringe, insert it into the powder vial and slowly inject all the solvent. Swirl gently without removing the syringe. Do not shake.
- Make sure the solution is clear and does not contain any particles.
- Turn the vial upside down and gently draw the solution back into the syringe by pulling the pump.
- Remove the syringe from the vial and place it on the table carefully. Do not touch the needle and do not let the needle touch any surface.



(If you are directed to inject more than one vial of GONAL-F, slowly re-inject the solvent into another powder vial, until you have dissolved the specified number of vials of powder into the solution. If you are required to inject Lutropin alfa in addition to GONAL-F, you can also mix the two medicines as an alternative to injecting each medicine separately. After dissolving the powder Lutropin alfa, draw the solution back into the syringe and inject it back into the vial containing GONAL-F. Once the powder has dissolved, draw the solution back into the syringe. Check if there are particles as before, and do not use if the solution is not clear. Up to three containers of powder may be dissolved in 1 ml of solvent.)

4. Preparing the syringe for injection:

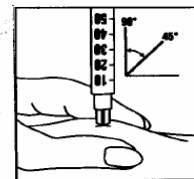
- Change the needle for the fine bore needle.
- Dispose of any air bubbles: If you see air bubbles in the syringe, hold the syringe with the needle pointing upwards and gently flick the syringe until all the air bubbles gather at the top. Push the plunger until the air bubbles disappear.



5. Injecting the dose:

- Inject the solution immediately. The doctor or nurse will have already advised you where to inject the solution (such as the stomach, the front of the thigh). To reduce skin irritation, select a different injection site each day.
- Clean the area of skin injected with alcohol swab.
- Pinch the skin firmly and inject the needle at a degree of inclination of 45 ° to 90 ° using a dart-like motion.
- Inject under the skin by pressing the plunger slowly, as taught by a doctor or nurse. Do not inject directly into a vein. Take as much time as you may need to inject all the solution.

- Immediately pull the needle out and clean the skin with the alcohol swab.



6. After injecting:

Dispose of all used items: Once you have finished your injection, immediately discard all needles and empty glass containers in the sharps container provided. Any unused solution must be discarded.