



Please read the leaflet carefully before you start to take this medicine.

This leaflet contains important facts about this medicine; do not discard this leaflet, you may need to refer to it again in the future.

- Consult your physician or pharmacist for further information.
- This medicine has been prescribed for your current condition; do not suggest this medicine to others as it may be harmful for them, even though they may share your symptoms.

In this leaflet you will find:

1. What is Cinnal-f® and what is it used for?
2. What should you consider before using Cinnal-f®?
3. How to use Cinnal-f®?
4. What are the common side effects of Cinnal-f®?
5. How to store Cinnal-f®?

Cinnal-f® 75 IU (equivalent to 5.5 micrograms) is presented as an injectable white powder along with its solvent for injection.

The active ingredient of Cinnal-f® is 75 IU (equivalent to 5.5 µg) of follitropin alfa that is synthesized from the Chinese Hamster ovarians cells through genetic engineering. Other ingredients of this product are: sucrose, sodium dihydrogen phosphate monohydrate, disodium hydrogen phosphate dihydrate, methionine, polysorbate 20.

This product is manufactured by Singapore Biotech.

1. What is Cinnal-f® and what is it used for?

Cinnal-f® is in form of a white lyophilized powder presented with its solvent which is water for injection.

Each box contains one sterile vial of lyophilized powder, one sterile vial of WFI.

Cinnal-f® is a recombinant human follicle stimulating hormone belonging to the Gonadotropins category.

Indications:

- Women who cannot ovulate and do not respond to treatment with clomiphene citrate can use Cinnal-f® to stimulate ovulation.
- Using Cinnal-f®, women undergoing IVF will develop several follicles (each containing an egg). The drug also assists in gamete intra-fallopian transfer.
- Together with another medicine called "lutropin alfa" (recombinant human Luteinising Hormone), Cinnal-f® stimulates ovulation in women who are not ovulating due

to low FSH and LH gonadotropins secretion.

- Together with other medicines such as human Chorionic Gonadotropin (hCG), Cinnal-f® helps producing sperms in men who are infertile due to a low level of sexual hormones.

2. What should you consider before use Cinnal-f®?

You and your partner's fertility should be evaluated before starting the treatment

Do not use Cinnal-f® in following cases:

- If you are allergic to Follicle Stimulating Hormone or any of the other ingredients of Cinnal-f®.

- If you have a tumour in your hypothalamus or pituitary gland.

women who have the following conditions:

- Large ovaries or cysts unrelated to polycystic disease.
- With unexplained vaginal bleeding.
- With cancer in ovaries, uterus or breasts.

- Men who have the following conditions:

use of Cinnal-f® in irreversible damaged testicles must be avoided.

Driving and activities that demand caution:

The effects of this medicine on the ability to drive or operate machineries have not been studied.

Warnings and recommendations:

- If you or any member of your family have porphyria (an inability to break down porphyries that may be passed on from parents to children), you must consult your physician before you begin the treatment as the use of this medicine may worsen the condition.

- If your skin becomes fragile and easily blistered, especially in uncovered areas, and/or you have stomach, arm or leg pain, consult your physician immediately as you may be recommend to stop the treatment.

- This treatment can increase the risk of developing Ovarian Hyper-Stimulation Syndrome (OHSS) in women (refer to the side-effects section). However, in case you are not ovulating, and if the recommended dose and schedule of administration are adhered to, the occurrence of OHSS is less likely. Cinnal-f® treatment seldom causes severe OHSS unless the medicine that is used for final follicular maturation (containing human Chorionic Gonadotropin, hCG) is administered. If you are developing OHSS your physician may not give you any hCG in this treatment cycle and you may be told not to have sex or to use a barrier contraceptive method for at least four days.

- In patients undergoing assisted reproductive technology the risk of having a multiple pregnancy is increased which of course is related to the number of fertilised eggs or embryos placed inside them.

- In such patients, the risk of miscarriage is higher than the average population, however, it is no significantly higher than women with fertility complications.

- There have been isolated reports of severe allergic reactions to Cinnal-f® (of course they were not that sever); however, if you notice any of these reaction when using

similar medicines, do inform your physician.

- Increased FSH levels in men depends on the degree testicle damage; of course Cinnal-f® is not effective in such cases. After 4 to 6 months after starting treatment, semen analysis is usually requested by the doctor for control purposes.

Use by pregnant and lactating women:

Use of Cinnal-f® is forbidden for pregnant and lactating women.

Important information about one of the ingredients of Cinnal-f®:

Cinnal-f® contains less than 1 mmol sodium (23 mg) per dose, therefore it is considered essentially sodium-free.

Important information about using Cinnal-f® in conjunction with other medicines:

Consult your physician if you are taking any other type of medicine; even for drugs that are sold without prescription. Based on the studies, the only medicine that can be used in together with Cinnal-f® is lutropin alfa.

3. How to use Cinnal-f®?

The dosage and the schedule of administration are to be determined by the physician.

Use Cinnal-f® exactly as your physician has prescribed. If you are not certain about how you should take the medicine, you should contact your physician or pharmacist. Also, you can consult your physician about the effectiveness of this medicine.

Dosage and length of usage of Cinnal-f®:

Women who do not ovulate or have irregular or no periods. Cinnal-f® is usually given every day. If you have irregular periods, start using Cinnal-f® within the first 7 days of your menstrual cycle.

The usual starting dose of Cinnal-f® is 75 to 150 IU per day; the dosage may be increased every 7 or every 14 days by 37.5 to 75 IU.

The maximum daily dose of Cinnal-f® is usually not higher than 225 IU.

After the desired effect has been achieved, it is recommended that you receive a single hCG injection 24 to 48 hours after your last injections of Cinnal-f®. It is also recommended that you have sex on the day of your hCG injection and the day after.

In case of sever response, the treatment is to be stopped and you will not be given any hCG (refer to side effects section). For the following cycle, your physician should prescribe you a lower dose of Cinnal-f®.

Women who need to develop several eggs for collection prior to any assisted reproductive technology

The usual starting dose of Cinnal-f® is 150 to 225 IU each day, from day 2 or 3 of menstrual cycle. Cinnal-f® dose may be increased, depending on patient response. Treatment is continued until patient egg have developed to a desired point (blood tests and/or an ultrasound machine) The

sufficient development of the follicle is on average achieved at the tenth day of the treatment (between day 5 and day 20). Injection of 10,000 IU of hCG, 24 to 48 hours after the last Cinnal-f® injection is recommended.

On the other hand, a lower dose of gonadotropin-releasing hormone (GnRH) can be prescribed as supplemental treatment; in that case, Cinnal-f® is started after two weeks. The Cinnal-f® and GnRH agonist are then both given until patient follicles develop as desired.

For example, after two weeks of GnRH agonist treatment, 150 to 225 IU Cinnal-f® is administered for 7 days. The dose is then adjusted according to patient ovarian response.

When GnRH antagonist is used, it is administered from the 5th or 6th day of Cinnal-f® treatment and continued until ovulation induction.

Women who are not ovulating, having no periods or have been diagnosed with very low levels of FSH and LH hormones.

The dosage and the schedule of administration are to be determined by the physician. The usual starting dose of Cinnal-f® until 3 weeks is 75 to 150 IU together with 75 IU of lutropin alfa.

Your dose of Cinnal-f® may be increased every 7 or every 14 days by 37.5 to 75 IU, until you get the desired response. When you get the desired response, you will be given a single injection of hCG, 24 to 48 hours after your last injections of Cinnal-f® and lutropin alfa. The best time to have sex is on the day of the hCG injection and the day after. Alternatively, intrauterine insemination (IUI) may be performed by placing the sperm into the womb cavity. If your doctor cannot see a response after 3 weeks, that treatment cycle with Cinnal-f® should be stopped. If your body responds too strongly (see section possible side effects), your treatment with Cinnal-f® will be stopped and you will be given a lower dose of Cinnal-f®.

Men with low reproductive hormones

The usual dose of Cinnal-f® for this group is 150 IU together with hCG 3 times a week for at least 4 months.

If the patient has not responded to treatment after 4 months, the physician may suggest that you continue using these two medicines for at least 18 months.

How is Cinnal-f® administered?

Cinnal-f® is intended for subcutaneous use. It is for single use only.

If you administer Cinnal-f® to yourself, please carefully read the following instructions.

– Wash your hands. It is important that your hands and the items you use be as clean as possible.

– Assemble and lay out on a clean surface everything you need:

One vial containing Cinnal-f® powder

One solvent vial

One syringe

One needle for reconstitution and a fine needle for subcutaneous injection.

Preparing the injectable solution

Remove the protective caps from the powder vial.

– Fill the syringe with solvent. put the needle of the filled syringe through rubber inside the vial. gently inject the full content of the syringe into vial. keeping the syringe attached to the vial, gently swirl the vial until all the powder has dissolved. avoid shaking the vial. Check that the resulting 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 plunger.

– Remove the syringe from the vial and set it down carefully, Do not touch the needle and do not allow the needle to touch any surface. (If you have been prescribed more than one vial of Cinnal-f®, slowly re-inject the solution into another powder vial, until you have the prescribed number of powder vials dissolved in the solution. If you have been prescribed lutropin alfa in addition to Cinnal-f®, you may also mix the two medicines as an alternative to injecting each product separately. After dissolving the lutropin alfa powder, draw the solution back into the syringe and re-inject it into the vial containing Cinnal-f®. Once the powder has dissolved, draw the solution back into the syringe. Inspect for 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.

– Change the needle for the fine needle. Remove 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 collects at the top. Push the plunger until the air bubbles are gone.

– Immediately inject the solution after reconstitution: Your physician or nurse will have already advised you where to inject (e.g. tummy or front of thigh). To minimise skin irritation, select a different injection site each day.

– Clean the chosen skin area with an alcohol swab using a circular motion. Firmly pinch the skin together and insert the needle at a 45° to 90° angle using a dart-like motion.

– Inject under the skin by pushing gently the plunger, as you were taught. Do not inject directly into a vein. Take as much time as you need to inject all the solution. Immediately withdraw the needle and clean the skin with an alcohol swab using a circular motion.

– After the injection Dispose of all used items: Once you have finished your injection, immediately discard all needles and empty glass containers.

If you use more Cinnal-f® than you should:

The effects of taking too much Cinnal-f® are unknown, nevertheless one could expect Ovarian Hyper-Stimulation Syndrome (OHSS) to occur (side effects section). However the OHSS will only occur if hCG is also administered (refer to warnings and recommendations)

If you forget to use Cinnal-f®:

If you forget to use Cinnal-f®, do not take a double dose to make up for a forgotten dose. Please talk to your physician as soon as you notice that you forgot a dose.

4- What are the common side effects of Cinnal-f®?

Like all medicines, Cinnal-f® can cause side effects.

– Common side effects are: Ovarian cysts, Headache, Local reactions at the injection site (such as pain, redness, bruising, swelling and/or irritation).

Following treatment with Cinnal-f® when hCG is administered, a condition called ovarian hyperstimulation syndrome (refer to warnings and recommendations) can occur. This syndrome is characterised by large ovarian cysts. The following are first symptoms of ovarian hyperstimulation: pain in the lower abdominal region, possibly in combination with nausea vomiting and weight gain.

Should the above mentioned symptoms occur, a careful medical examination is indicated as soon as possible. In serious (rare cases), an ovarian hyperstimulation syndrome with clearly enlarged ovaries, can go hand in hand with possible accumulation of fluid in the abdomen or thorax as well as ovarian torsion or more serious thromboembolic complications.

In rare cases the latter can also be found independently of ovarian hyperstimulation syndrome.

In view of the above, to prevent such events, when the ovarian response is excessive, treatment with Cinnal-f® could be discontinued by your physician and the treatment with hCG abandoned.

Rarely abnormal blood clotting have been seen to occur with similar medicines. Therefore, this could possibly occur with Cinnal-f® / hCG or lutropin alfa/ Cinnal-f® / hCG.

In rare cases, (mild) allergic reactions have been reports.

– Pregnancy where the embryo is implanted outside the womb (ectopic pregnancy) may occur especially in women with a history of prior tubal disease.

– Following treatment with hCG, men can develop enlarged breasts, acne, or weight gain.

If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your physician or pharmacist.

5. How to store Cinnal-f®?

Keep out of the reach and sight of children.

Store in temperatures between 2 to 8 °C away from direct sunlight.

Protect from freezing.

Do not use the medicine past its expiry date.

The medicine must be administered immediately after reconstitution.

Do not use the medicine if you notice any visible signs of deterioration.

The reconstituted solution should not be administered if it contains particles or is not clear.