PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

Zivafert PFS 5000 IU

powder and solvent for solution for injection

Human chorionic gonadotropin

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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, please 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.
- In this leaflet Zivafert PFS 5000 IU powder and solvent for solution for injection is called Zivafert PFS.

What is in this leaflet:

1. What Zivafert PFS is and what it is used for
2. What you need to know before you use Zivafert PFS
3. How to use Zivafert PFS
4. Possible side-effects
5. How to store Zivafert PFS
6. Contents of the pack and other information

1. What Zivafert PFS is and what it is used for

What Zivafert PFS is:

Zivafert PFS contains human chorionic gonadotrophin, a hormone obtained from human urine, belonging to the "gonadotropin" family, which are natural hormones involved in reproduction and fertility.

What Zivafert PFS is used for:

Zivafert PFS is used:
- To help develop and ripen several follicles (each containing an egg) in women undergoing

assisted reproductive technologies (procedure that may help you to become pregnant) such as 'in vitro fertilisation' (IVF).
• To help release an egg from the ovary (ovulation induction) in women who cannot produce eggs ('anovulation'), or women who produce too few eggs ('oligo-ovulation').

This medicinal product must be used under the supervision of your doctor unless you are told otherwise by your doctor.

2. What you need to know before you use Zivafert PFS

Do not use Zivafert PFS if you:
- are allergic to the human chorionic gonadotropin or any of the other ingredients of this medicine (listed in section 6)
- have untreated diseases involving thyroid, pituitary or adrenal glands
- have ovarian, womb or breast cancer
- have a condition that makes a normal pregnancy impossible, e.g. ovarian failure, absence of a uterus, premature menopause, fallopian tube obstruction, fibroids in the womb or other abnormalities of the reproductive organs
- have recently had unexplained vaginal bleeding.

Tell your doctor or pharmacist if you have any of the above because this medicine might not be the right medicine for you.

Warnings and precautions
Before the treatment, your doctor should have checked that your reproductive organs are normal.

Talk to your doctor before taking Zivafert PFS if you suffer from, or have suffered in the past from any of the following conditions:
- abnormalities of the reproductive organs
- long-term disease (such as diabetes, cardiovascular disorders etc.).
- vascular complication (i.e. increased risk of blood clots, previous or family history of blood clots, overweight).

Medical examinations
For up to ten days after administration of Zivafert PFS, a pregnancy test may give a false-positive result.

During therapy with Zivafert PFS the following can occur:

Ovarian hyperstimulation syndrome (OHSS)

Treatment with gonadotropic hormones like Zivafert PFS may cause ovarian hyperstimulation syndrome (OHSS). This is a serious medical condition where the ovaries are overly stimulated and the growing follicles become larger than normal. In rare cases, severe OHSS may be life-threatening. Therefore, close supervision by your doctor is very important. To check the effects of treatment, your doctor will do ultrasound scans of your ovaries. Your doctor may also check blood hormone levels (See also section 4. 'Possible side effects').

OHSS causes fluid to build up suddenly in your abdominal (stomach) and chest areas and can cause blood clots to form. Call your doctor right away if you have:
- severe swelling and pain in the stomach area (abdomen)
- feeling sick (nausea)
- vomiting
- sudden weight gain due to fluid build-up
- diarrhoea
- decreased urine output
- trouble breathing.

Ovarian torsion

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, it is important to inform your doctor if you:
- have ever had 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.

Blood clot (thrombosis)

Being pregnant increases the chance of having a blood clot.

If you have risks factors for having a blood clot (for example being overweight, or you have a family history of blood clots), the chance of having a blood clot in a blood vessel may be increased during IVF treatment.

Blood clots can lead to serious medical conditions, such as:
- blockage in your lungs (pulmonary embolus)
- stroke
- heart attack
- reduced blood flow to the vital organs that may result in organ damage
- reduced blood flow (deep vein thrombosis) to your arm or leg that may result in a loss of your arm or leg.

Multiple births, birth defects, miscarriage or pregnancy complications

If treatment with Zivafert PFS results in pregnancy, there is an increased chance of having twins or multiple births. Multiple pregnancies carry an increased health risk for both the mother and her babies around the time of birth. In women undergoing fertility treatment there is a slight increased risk of a miscarriage, or 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. Multiple births are more likely if you are taking other drugs that encourage ovulation (e.g. hMG).

It is unknown if IVF treatment causes congenital malformations, or some cancers of the sex organs.

Children and Adolescents
The product is not to be used by children or adolescents.

Other medicines and Zivafert PFS
Tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including any without a medical prescription. This is particularly important if you are taking drugs that:

- stimulate ovulation (e.g. hMG)
- contain cortisone, especially high doses.

Pregnancy and breastfeeding
Do not use Zivafert PFS if you are pregnant or breast-feeding. If you think you may be pregnant, ask your doctor for advice before taking this medicine.

Driving and using machines
Zivafert PFS does not alter your ability to drive vehicles or use machines.

Zivafert PFS contains sodium
This medicine contains less than 1 mmol of sodium (23 mg) per reconstituted solution, that it is essentially 'sodium free'.

3. How to take Zivafert PFS

Zivafert PFS is a powder to be dissolved with a liquid (solvent) before use; it is given by injection under the skin (subcutaneously) or into a muscle (intramuscularly). The solution is obtained by combining the solvent with the powder and must be used immediately after preparation.

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

How Zivafert PFS should be given:
Zivafert PFS is given by injection under your skin (by the subcutaneous route) or into your muscle (intramuscular injection).

Each vial should be used only once and the injection should be used as soon as it is prepared.

The recommended dose of Zivafert PFS is 5000 I.U. or 10000 I.U. to be administered 24-48 hours after optimal stimulation of follicular growth is achieved.

After suitable advice and training your doctor may ask you to inject Zivafert PFS yourself.

For the first time, your doctor must:

- have explained how to prepare the right dose of injection
- have shown you how to prepare the solution for injection
- have shown you the possible places where you can inject yourself
- let you practise giving yourself a subcutaneous injection.

Before injecting Zivafert PFS yourself, read the following instructions carefully.

How to prepare Zivafert PFS using 1 vial of powder

The solution must be prepared just before injection. Each vial is for single use only.

Zivafert PFS must only be made up with the solvent provided in the pack using the following step-by-step instructions:

Step 1

Wash your hands before preparing the solution. Use a clean surface for preparation. It is important that your hands and the items you use are as clean as possible.

Step 2

Set out all the following items on the clean surface:
- two cotton wool alcohol swabs (not provided in the pack)
- one vial containing Zivafert PFS powder
- one solvent in a prefilled syringe
- one long needle for the reconstitution and for the intramuscular injection
- one short needle for the subcutaneous injection.

REMEMBER Please do not remove the back-stop (white collar) from the prefilled syringe since it prevents inadvertent withdrawal of the stopper and improves syringe handling during the injection.

Step 3



- Remove only the cap from the prefilled syringe.
- Apply the reconstitution needle (long needle) with its protective cap attached, on the syringe and check if the needle is well allocated, in order to avoid leaking of solution. In case of leaking of solution please try to fix better the needle with a slight rotation.
- Carefully place the syringe on the clean surface.
- Avoid touching the needle.

Step 4



- Remove the coloured plastic cap from the Zivafert PFS vial by gently pushing it upwards.
- Wipe the rubber top with an alcohol swab and allow to dry.

Step 5



- Pick up the syringe, remove the protective cap of the needle and push the needle through the rubber middle of the Zivafert PFS vial top.
- Press the plunger down firmly and slowly inject the solvent into the powder vial through the rubber stopper, to squirt all the solution into the vial containing the powder.

- **DO NOT SHAKE, gently roll the vial between the hands until the powder is completely dissolved, taking care to avoid creating foam.**

Step 6



Once the powder is dissolved (which, in general, occurs immediately), slowly draw the solution into the syringe as described below:

- With the needle still inserted, turn the vial upside down.
- Make sure the needle tip is underneath the level of the liquid.
- Gently pull the plunger to draw all the Zivafert PFS solution up into the syringe.
- Check that the reconstituted solution is clear and colourless.

Preparation of higher doses, using more than 1 vial of powder

If your doctor has recommended the 10000 IU higher dose for you, this can be achieved by using two vials of powder with one prefilled syringe of solvent.

When making up 2 vials of Zivafert PFS, at the end of step 3 above, draw back the reconstituted contents of the first vial into the syringe and slowly inject into a second vial. Repeat steps 4-6 with the other vial.
The solution must be clear and colourless.

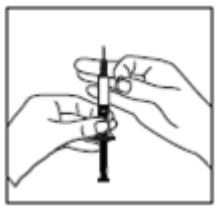
Injecting your medicine intramuscularly:

For intramuscular injections your doctor or nurse will prepare and then inject Zivafert PFS into the side of your thigh or buttock.

Injecting your medicine subcutaneously

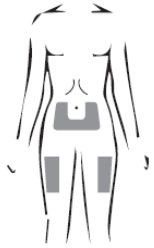


- When the syringe contains the correct dose for you, attach the protective cap of the long needle. Remove the long needle from the syringe and replace it with the short needle for subcutaneous injection with its protective cap attached. Please be aware that the needle is well allocated and push the short needle firmly onto the syringe barrel, then twist it slightly to ensure it is fully screwed on, to create a firm seal in order to avoid leaking of solution.

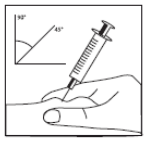


- Remove the protective cap of the needle. Hold the syringe with the needle pointing upwards and gently tap the side of the syringe to force any air bubbles up to the top.
- Push the plunger until a bead of liquid appears at the tip of the needle.
- **DO NOT USE the solution if it contains any particles or is cloudy.**

The injection site:



- Your doctor or nurse will have already advised you, where on your body to inject the medicine. The usual places are the thigh or the lower abdominal wall (stomach area), below the navel.
- Wipe the injection site with an alcohol swab.
- Firmly pinch the skin together. With the other hand, insert the needle with a dart-like motion at an angle of 45° or 90°.



Injecting the solution:

- Inject under the skin as shown by your doctor.
- Do not inject directly into a vein.
- Push the plunger slowly and steadily, so the solution is correctly injected and the skin tissues are not damaged.

Take as much time as you need to inject the volume of solution prescribed.

Removing the needle:

- Pull the syringe out quickly and apply pressure to the injection site.
- A gentle massage of the site – while still maintaining pressure – helps disperse the Zivafert PFS solution and relieve any discomfort.

Dispose of all used items:
Once you have finished your injection, all the needles and empty syringes should be disposed of in an appropriate container. Any unused solution or waste material should be disposed of in accordance with local requirements.

If you use more Zivafert PFS than you should:
The effects of an overdose of Zivafert PFS are unknown, nevertheless, one could expect ovarian hyperstimulation syndrome to occur (see 'Possible side effects'). If you use more Zivafert PFS than you should, speak to your doctor or pharmacist.

If you forget to use Zivafert PFS:
If you forget to use Zivafert PFS immediately contact your doctor.

If you stop using Zivafert PFS:
Consult your doctor if you are considering to not use this medicine.

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

4. Possible side effects

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

Stop using Zivafert PFS and see a doctor straight away if you notice any of the following serious side effects – you may need urgent medical treatment:

- mild or moderate excessive stimulation of the ovaries (ovarian hyperstimulation syndrome), which manifests as enlargement of the ovaries, ovarian cysts, abdominal pain with vomiting and nausea (see also in section 2. under "Ovarian hyperstimulation syndrome"). This is a common side effect (may affect up to 1 in 10 people).
- severe excessive stimulation of the ovaries (ovarian hyperstimulation syndrome) characterized by pain in the lower abdomen (pelvis), nausea, vomiting, increase in weight, accumulation of fluids in the abdomen (ascites) or chest (pleural effusion). This event is uncommon (may affect up to 1 in 100 people).
- ovarian cyst rupture (as a rare consequence of severe OHSS, may affect up to 1 in 1,000 people)
- formation of clots in the blood vessels (thromboembolic events), as a complication of ovarian hyperstimulation syndrome. This) event is rare (may affect up to 1 in 1,000 people)
- severe generalized allergic reactions which may include: swelling of face, eyes, lip, throat or tongue, breathing difficulties, wheezing, skin rash rare side effect (may affect up to 1 in 1,000 people)

Other side effects

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

- Injection site reaction which may include redness, bruising, swelling, itching or pain at the injection site
- swelling (oedema)
- mood changes
- headache
- painful breast

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

- restlessness (agitation), tiredness

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

- swelling in the deep layers of the skin, often seen with urticaria (hives)
- generalised skin rashes

If you experience any of the rare side effects indicated above, contact your doctor immediately who will assess whether to stop treatment with Zivafert PFS or immediately go to the nearest hospital casualty department.

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 via the Yellow Card Scheme www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Zivafert PFS

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

Do not store above 25°C. Keep the vial and the solvent in prefilled syringe in the outer carton in order to protect from light.

Use immediately after making up the solution.

Do not use this medicine after the expiry date which is stated "after EXP" on the outer carton, the vial and the prefilled syringe of solvent. If the expiry date is reported as month/year, the expiry date refers to the last day of that month.

Do not use Zivafert PFS if you notice the solution does not look clear (cloudy or with presence of visible particles). After being made up the solution must be clear and colourless.

Do not throw away any medicines via wastewater. 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 Zivafert PFS contains
The active substance is: human chorionic gonadotropin.

The excipients in the:
- vial of powder: lactose monohydrate
- prefilled syringe with solvent (0.9% sodium chloride): water for injections, sodium chloride.

Each vial contains: human chorionic gonadotropin 5000 IU, produced from human urine.

What Zivafert PFS looks like and contents of the pack
Zivafert PFS is presented as:
Powder in vial: white to almost white lyophilized powder
Solvent in pre-filled syringe (0.9% sodium chloride): clear and colourless solution

One single pack contains:
Plastic tray including powder in a vial (type I glass), sealed with a rubber closure and held in place with a flip-off cap.
1 ml of solvent in a pre-filled syringe (type I glass), 1 long needle for the reconstitution and for the intramuscular injection and 1 short needle for the subcutaneous injection.

Multipack containing 10 plastic trays, as described above.

Not all pack sizes may be marketed.

Marketing Authorisation Holder:
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Manufacturer:
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder via medinfo.uk@ibsagroup.com.

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