

IVF
Information
Brochure
(GNRH ANTAGONIST)



Dr Scott Salisbury
Obstetrician & Gynaecologist
Watkins Medical Centre
Level 3 225 Wickham Terrace
Brisbane Q 4000

Appointments 07 3010 2121
After Hours 07 3899 4455

IVF Antagonist Cycle

These information sheets are designed as a guide for your forthcoming IVF treatment cycle. They can be used to help you understand what will occur during the IVF cycle and also as a reference throughout the cycle if you are unsure of the next step in your treatment.

In your IVF treatment cycle you will be given two groups of drugs:

The first group are called Gonadotrophin Releasing Hormone (GnRH) drugs. The two drugs that may be used are **CETROTIDE** or **ORGALUTRAN**. These are given either in the form of a subcutaneous injection which is usually taken once daily. During normal cycles, the release of an egg depends on a hormone made by the pituitary gland. This is called *Luteinising Hormone*.

These drugs block the release of this hormone so that premature ovulation and subsequent loss of the egg cannot occur. Treatment with these drugs can cause some side-effects which include hot flushes, headaches and irregular vaginal bleeding. These are usually not a problem, are transient in nature and are no cause for concern. Once these drugs are stopped, the pituitary gland quickly recovers its normal function.

The second drug is called **Puregon or Gonal-F** (Pergonal, HMG , Metrodin 75, Metrodin HP, or Humagon 75 are the older versions) (these are just different names for the same drug-FSH). These drugs are used to stimulate the ovaries to produce follicles and, hopefully, eggs. They are dispensed in the form of injections, given subcutaneously by specially developed pens.

You will be told the dose of FSH to have when you are ready to start this part of your treatment. It does not normally have any side-effects. There are three basic regimens: "*long downregulation*" which requires you to start your Synarel or Lucrin on Day 20 of your cycle preceding your IVF attempt and "*short regimen*", which involves starting Synarel on Day 2 of your menstrual cycle. Alternative there is the regimen described here which is called an **ANTAGONIST CYCLE**..

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ANTAGONIST CYCLE PROTOCOL

YOUR CYCLE : What Happens

Last week of your menstrual cycle prior to your IVF or GIFT attempt

Please ring my secretary prior to Day 26 to let us know that you are starting with your next cycle. (if your cycle is longer than 30 days, let me know as this may affect planning).

Remember Day 1 is the first day you wake with your period. If your bleeding starts later in the day, the following day is Day 1.

Early in your treatment you should:

1. Register for treatment on the first floor of Watkins Medical Centre
2. Pay your booking and registration fee
3. Pay the fee for micro-injection, hatching, embryo glue etc if appropriate
4. Please also make sure that we have your home and/or work telephone number where you can be contacted during the day.

The actual cost at the time of treatment can be confirmed by telephoning the QFG office.

You will be asked to sign consent forms for your treatment at this time. We will also provide a drug request for so the cost of drugs can be met by medicare.

Please ring my office on 07 30102121 to make an appointment to be seen in the first 6 days of your cycle when you period arrives.

By Day 2 of your treatment cycle you and your partner will be taught how to administer the injections. Alternatively, arrangements can be made on a daily basis to have this performed at Watkins Medical Centre. Please note that because IVF is covered by a global fee which includes all ultrasounds, blood tests and administered drugs, you cannot go to your GP and have these administered under Medicare.

You will be informed of the dose you will need and appropriate amounts of drugs given to allow you to continue administering these yourself.

FSH can occur in many doses dictated by the pen in use.

You will have a blood test on Day 2 and occasionally a scan early in your treatment to check whether your body's control of the ovaries has been suppressed if your past history were to suggest that this might be the case. This scan is usually a vaginal (internal, empty bladder) scan. You will start your FSH on Day 2 of your treatment cycle. It is therefore important that you have your blood test at QFG on day 2 early and ring for the result between 12-2pm on weekdays, if it is likely to fall on a weekend you should ring me on day 1 to discuss how you may get your drugs remembering that you need to start your FSH on day 2.

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Please again make sure we have a contact number for you at all times, particularly on the weekends. During the week days *you* should ring my rooms (between 12 and 2pm) any weekday you have a blood test to find out the result if I request that you do so. Instructions will then be given as to when you should return for further review, whether you should change your dose, or possibly when you are ready for your egg collection. If it is the weekend, I will contact you or, alternatively, if that does not happen, please ring me at home at 7pm sharp, as I am occasionally away on the weekend. Please follow any message on the answering machine to obtain your result.

You will have another blood test (LH, Progesterone and Oestradiol) on Day 6 of your FSH treatment (Day 7 of your cycle). This blood test will again be performed on the first floor at QFG. On the basis of this blood test, we may change the dose of FSH. You will often have a scan on this day as well and these will be pre-arranged when you first get your drugs. This is very important as this determines when we would start your GNRH ANTAGONIST drug (orgalutran or cetrotide) . It is CRITICAL that no more than 24 hours at any one time elapses between doses of your ANTAGONIST drug. There is an extra cost to these drugs over and above the fee paid to QFG (up to \$100/day). These drugs will continue daily up until your hcg trigger.

You will need to continue with the daily injections of FSH on Days 7,8,9 etc (Days 12,13,14 etc) of your cycle.

Most ladies will have a further vaginal scan before the decision is made as to when the egg are to be collected.

Further blood tests and scans may be required depending on your individual response.

Eventually, you will be ready for your egg collection (approximately 10 -16 days after starting your FSH). This usually means 3 or more follicles greater than 17mm in diameter and Oestrogen levels consistent with this picture.

If it becomes obvious that not enough follicles are developing, or that the blood Oestrogen levels are not high enough and the chances of pregnancy in that particular cycle are very poor, then it may be necessary to stop all treatment and start again after the next period on a higher dose of FSH. This decision is very important as not only is it very disappointing for you, but it is also important to remember there is no point in persisting in that cycle unless you have a good prospect of pregnancy.

Occasionally, the treatment also has to be stopped because the ovaries are becoming too stimulated and to go on would be a risk to your health. This is called OVARIAN HYPERSTIMULATION. You should report any abnormal pain or sickness as these may be signs that excessive stimulation is occurring. These complications can occur but usually only occur in less than 5% of cycles.

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When you have enough follicles and your blood Oestrogen level is adequate, we will say that you are ready for your egg collection and arrange for you to have a special evening injection to induce ovulation (the timing is critical). This is necessary for the final maturation process of the egg. The timing of your egg collection will also be arranged at this time.

'Evening HCG Injection'

A time is arranged for a late night injection of HCG (a hormone which finally matures your eggs). This is done by the the person who usually gives you your other injections at home. The injection is normally given 37 hours before your planned egg collection and must be given at the time that I tell you. It should be given subcutaneously as you have been doing for the FSH. Ovidrel 250mcg/0.5ml is usually given to initiate ovulation. This comes in a prepackaged syringe. Alternatively, 2 Ampoules of HCG powder (Pregnyl) 5000U can be given and should be mixed with 1 ampoule of water ie 10,000U in total .

After this injection ***no more Antagonist (Cetrotide or Orgalutran), no blood tests or further scans are required.***

The following day you have a day off drugs in preparation for your egg collection the next day!!! QFG Day theatres will usually ring you the day before your planned surgery to confirm the arrangements with regard to where you need to go, what you need to bring and the appropriate time for you to arrive (make sure you have given them an appropriate contact number). Please remember to obtain, fill out and take with you your pre-admission forms for the day theatres.

EGG COLLECTION

Both partners should attend the QFG Day Theatres 1.5 hours before your egg collection if you are having IVF and 2 hours before your procedure if you are having GIFT.

It is important that you have nothing to eat or drink (including water) for 6 hours prior to your procedure.

The anaesthetist checks that you are fit for the planned operation.

A general anaesthetic will usually be administered for your procedure. You will normally be able to go home later the same day. You must be picked up from the hospital and someone should remain with you for the evening.

I would also strongly advise that if you live more than 100kms from Brisbane, you make arrangements to stay in Brisbane overnight.

If you are having IVF, your partner's sperm will be collected within a few hours of your egg collection and processed. Your eggs will be inseminated approximately 2-4 hours after egg collection. With GIFT, the sperm sample will need to be collected prior to egg collection. Ideally, the sample should be collected after 2-5 days (and probably no longer than a week) of abstinence, by masturbation performed either at home or at the QFG Day Theatres. If you believe there may be a problem with collection, you should let me know in advance.

Fertilisation will be apparent the following morning and you will be asked to ring my rooms to see how you fared in terms of fertilisation and to arrange a time for your embryo transfer to be performed. Embryo transfer will then be performed 2-5 days later if fertilisation has occurred.

Although all eggs are placed with sperm, only 60-70% of eggs will usually fertilise (to produce an embryo). With GIFT, eggs and sperm are put back immediately following the egg collection via laparoscopy (under the one anaesthetic) and the remaining eggs are then fertilised in the laboratory as in the case of IVF.

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EMBRYO TRANSFER

You should attend the QFG Day Theatres at the stated time (going straight to the 4th floor on this occasion). This will be 2-5 days after the egg collection.

You will be informed of the number of eggs which have been fertilised at this time and after a discussion, a decision will be made as to the number of embryos to be put back. This depends on the number available, your age and previous fertility, the quality of the embryos and what has happened in previous cycles. (the choice is between 1 and 2 only)

Transferring more than one embryo increases the chance of pregnancy occurring but this also increases the chances of multiple pregnancy. Multiple pregnancy, especially of more than two foetuses, has a higher rate of miscarriage, premature birth and operative delivery. There are also practical, emotional and financial implications to be kept in mind.

For these reasons in the vast majority of patients I will transfer **1 or 2 embryos**, choosing the best from those that are available. If excess embryos are available for freezing, this will be discussed with you at the time. Only the best embryos are suitable for freezing as poorer quality embryos do not survive the freeze-thaw cycle well. There is also an extra fee for this service if embryos are stored for more than 6 months. Therefore, freezing is usually the exception rather than the rule. The embryo transfer is performed in the QFG Day Theatres. It is essentially a similar procedure to having a smear test performed. You will not need an anaesthetic for this and therefore do not need to be starved. You will be asked to rest for 30 minutes after the procedure but can then go home and carry on life as normal. You should not, however, have intercourse for 10 days following your egg collection.

You will usually be given Crinone (a Progesterone gel) to use vaginally daily, or Progesterone pessaries. Alternatively two or three booster injections of HCG may be given every few days following your embryo transfer. You may also be asked to take Progynova (oestragen) and Provera (progesterone) tablets depending on your individual circumstance. Aspirin in 100mg tablets (Baby aspirin – Cardiprim) is sometimes also prescribed.

After this, all we can do now is wait - it is probably the most difficult time in the IVF cycle.

You will be asked to give a sample of blood for a pregnancy test 14 days after your embryo transfer or GIFT procedure if your period has not come. Forms are usually given to you when I give you the paper work for the day theatres. Results are available 60 minutes after the blood test is performed.

A positive result

If the result is positive, I will ask you to have another blood test in 48 hours and if it confirms a good rise in your pregnancy levels I will get you come for a vaginal scan in two and a half weeks time. Please make an appointment with my secretary when you ring for your second blood result. You will need to stay on all your medication until approximately 10 weeks of pregnancy. This scan is to establish if the pregnancy is in the correct position within the uterus, whether it is viable and how many sacs there are.

A negative result

A negative result on Day 14 after transfer means that the cycle has not worked this time and you should make an appointment to see me to review your cycle and future plans. If you have had no bleeding by Day 21, then you should repeat your pregnancy test on that day.

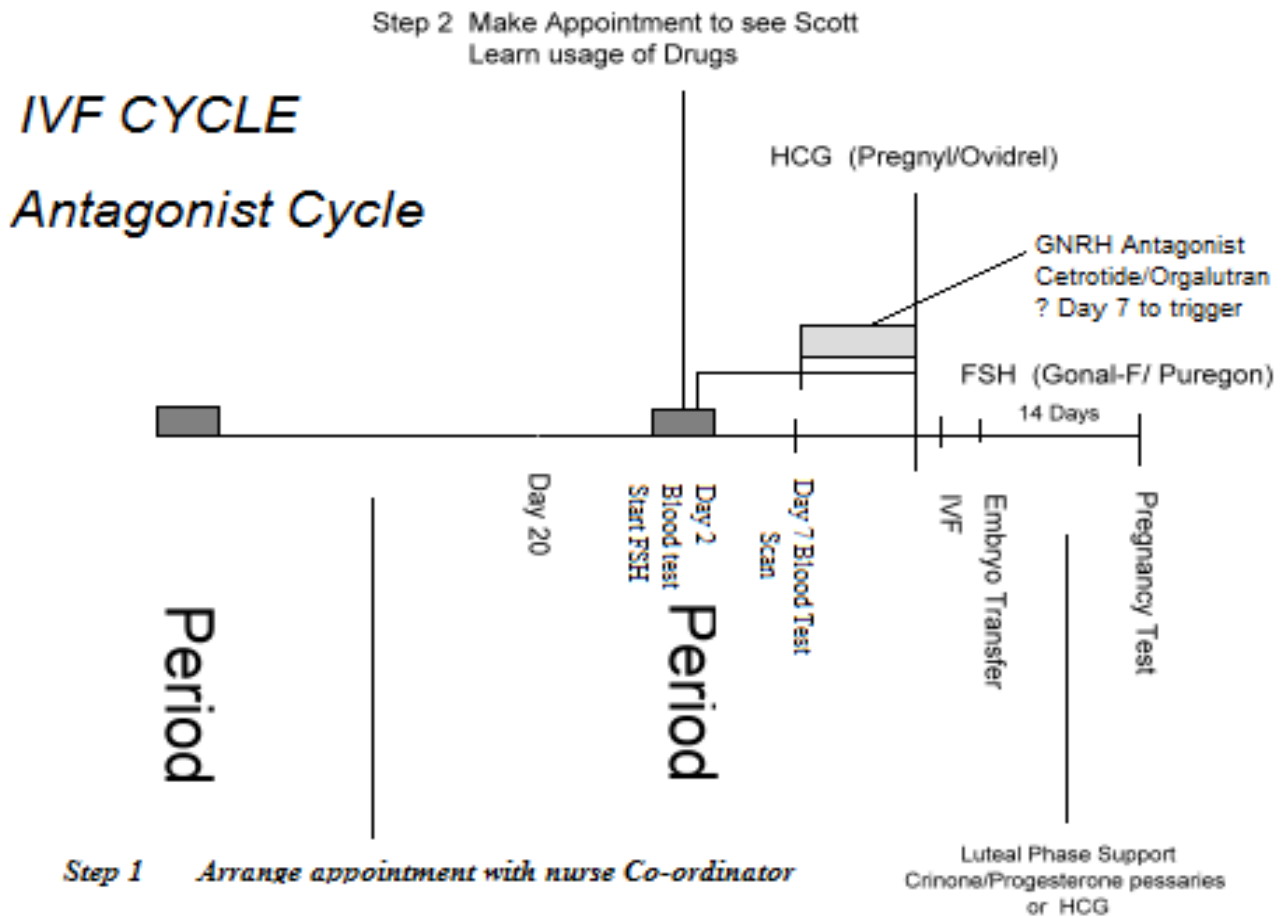
This leaflet is brief but hopefully may help you during your cycle to understand what will be required of you.

GOOD LUCK!

Scott Salisbury

IVF Antagonist Cycle

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- Step 1** *Arrange appointment with nurse Co-ordinator*
- Step 2** *Blood Test Day 2 QFG*
You will need to arrange to either get your drugs on this day or prior to day 2 preferably by making an appointment to see Scott
Arrange payment of QFG expenses

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IVF FLOW CHART

Day 2

Make Appointment with rooms prior to Day 2
visit **QFG office** on the **1st floor** :
pay fees and obtain drugs before Day 2
Blood Test Day 2 (FSH LH Prog E2)



Commence FSH Day 2 of treatment cycle



Day 6 FSH (Day 11 of your cycle) **Blood test +/- Scan**
? start cetrotide or orgalutran at this stage



Day 8/9 FSH (Day 13/14 of your cycle) **Scan**



adequate no. of follicles and appropriate amount of Oestrogen
measured on your blood test
(between 10-20 days)



evening HCG injection

37 hours before egg collection
Crinone / Pregnyl
cease cetrotide or orgalutran & FSH only at this time



Egg Collection QFG day OT **Sperm Collection**



Ring for results of fertilisation
24 hours later



Embryo transfer

2-5 days after egg collection



Pregnancy Test
14 days following egg collection



negative
further review
? ivf again



positive
ultrasound 2.5
weeks following



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Glossary

Intracytoplasmic Sperm Injection (ICSI)

Intracytoplasmic sperm injection (ICSI) is a laboratory procedure developed to help infertile couples undergoing in vitro fertilization (IVF) due to male factor infertility. ICSI, a form of micromanipulation, involves the injection of a single sperm directly into the cytoplasm of a mature egg (oocyte) using a glass needle (pipette). This process increases the likelihood of fertilization when there are abnormalities in the number, quality, or function of the sperm. ICSI is generally unsuccessful when used to treat fertilization failures that are primarily due to poor egg quality.

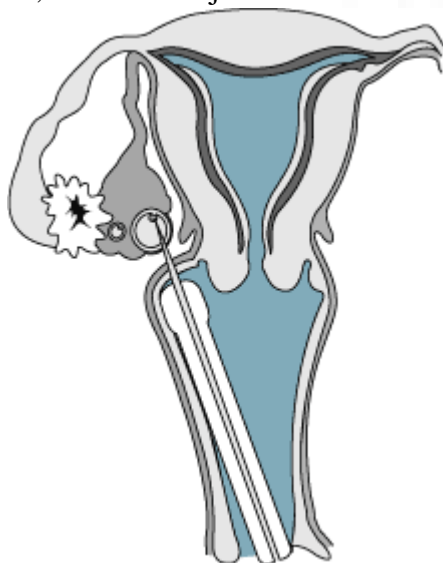
A variety of abnormalities can cause male infertility. Sperm can be completely absent from the ejaculate (azoospermia) or present in low concentrations (oligospermia). Sperm may have poor motility (asthenospermia) or have an increased percentage of abnormal shapes (teratospermia). There may also be functional abnormalities which prevent the sperm from binding to and/or fertilizing the egg.

Indications for Intracytoplasmic Sperm Injection

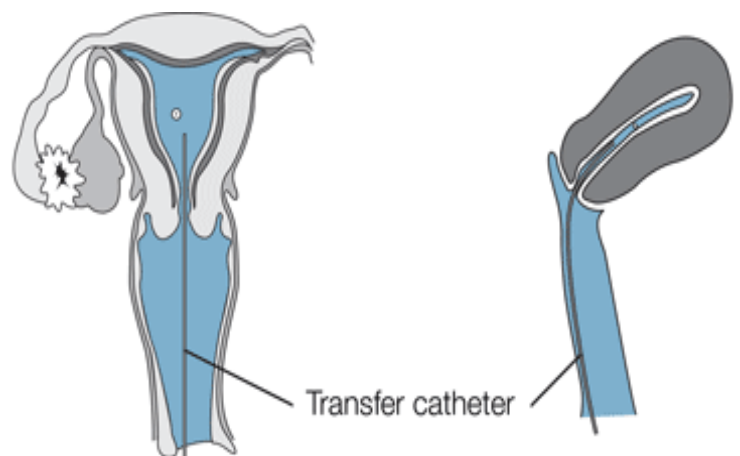
- Very low numbers of motile sperm.
- Severe teratospermia.
- Problems with sperm binding to and penetrating the egg.
- Antisperm antibodies thought to be the cause of infertility.
- Prior or repeated fertilization failure with standard IVF methods.
- Frozen sperm limited in number and quality.
- Obstruction of the male reproductive tract not amenable to repair. Sperm may then be obtained from the epididymis by a procedure called microsurgical epididymal sperm aspiration (MESA), or from the testes by testicular sperm aspiration (TESA).

Fertilization occurs in 50% to 80% of injected eggs. The ICSI process may damage a small percentage of eggs. The fertilized egg may fail to divide, or the embryo may arrest at an early stage of development. Pregnancy rates are comparable to rates seen with traditional IVF. Younger patients may achieve even more favourable results. Factors such as poor egg quality and advanced maternal age may result in lower rates of success.

ICSI does not increase the incidence of multiple gestation as compared to standard IVF. Because ICSI is a relatively new technique, first performed in 1992, long-term data concerning future health and fertility of children conceived with ICSI is not as comprehensive as standard IVF but what data is available is reassuring. This is an area of ongoing investigation. Because some causes of male infertility are familial and are related to genetic problems, male offspring might have reproductive problems as adults. Despite these concerns, ICSI is a major advance in the treatment of severe infertility.



Egg Collection



Embryo Transfer

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Options for numbers of embryos transferred

There is uncertainty in deciding the number of embryos to transfer in an IVF cycle. So far, information on single embryo transfer is very limited. The chance of a twin pregnancy conceived naturally is about 1:80 births, so the risk of conceiving a multiple pregnancy in IVF is significantly increased (about 20% if two embryos are transferred).

This is why most fertility clinics have reduced the absolute number of embryos transferred to two. The question is whether we should limit the embryo transfer to one?

Risks associated with multiple pregnancy

IVF specialists agree that the risk of multiple pregnancy needs to be reduced in IVF practice. Potential problems for babies include:

- low birth weight
- premature birth
- higher risk of cerebral palsy
- serious complications after birth, including infant mortality
- increased speech and reading problems among "toddler" twins.

Potential problems for the parents include:

- high blood pressure during pregnancy
- post partum haemorrhage
- fatigue and sleep deprivation
- financial pressure on the family.

The decision about how many embryos to transfer will be based on age, number of attempts, previous fertility, reasons for infertility and embryo quality.

It is important that if you wish to reduce the risk of multiple pregnancy that you inform me that you only wish one embryo to be returned.

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GNRH ANTOGONISTS ORGALUTRAN / CETROTIDE

WHAT ARE GNRH ANTAGONISTS ?

They are injectable drugs that controls hormonal responses in your body, which impacts on the development of eggs in your ovaries. Specifically, Cetrotide/Orgalutran helps to prevent a hormonal event known as the "LH surge". It is a very important part of the ovarian stimulation cycle you have established with your doctor.

WHAT IS THE LH SURGE AND HOW DOES IT AFFECT INFERTILITY?

The LH surge is a natural hormonal response that signals the release of mature eggs from an ovary. However, if an LH surge occurs too early in a cycle, eggs are released before they can fully mature. This greatly reduces the opportunity to retrieve the eggs for later use in assisted reproductive technology (ART) procedures. The LH surge is caused by a series of changes involving 2 hormones: gonadotropin-releasing hormone (GnRH) and luteinizing hormone (LH). When GnRH is present, it triggers a dramatic rise or "surge" in LH levels.

HOW DOES CETROTIDE/ORGALUTRAN PREVENT THE LH SURGE?

Cetrotide/Orgalutran work by directly blocking the trigger effect of GnRH. This blocking action stops a possible LH surge before it begins, allowing eggs to reach the level of development needed for fertilization. Because of the way it works, Cetrotide/Orgalutran are therefore called GnRH antagonists.

WHEN SHOULD YOU USE CETROTIDE/ORGALUTRAN ?

You only need to use Cetrotide/Orgalutran for the short part of your cycle in which a LH surge is a concern. This is the part of your cycle when your eggs are nearing maturity, but are not yet ready for fertilization. Cetrotide/Orgalutran administration should be started either on the morning of stimulation day 6 or according to your scans prediction of when an LH surge may be initiated.

WHICH DOSING REGIMEN OF CETROTIDE/ORGALUTRAN SHOULD YOU USE?

Orgalutran is available in 1 dose 250 µg

Cetrotide® is available in 2 dosing regimens: a single dose (3 mg), which controls the LH surge for up to 4 days, or a daily

dose (0,25 mg) at 24 hour intervals over a short period of time. When using Cetrotide® 0,25 mg, the injections should be given in 24 hour intervals which should not be exceeded. Your doctor has chosen the regimen that best meets your individual needs. Be sure to follow your doctor's specific instructions for dose strength and schedule.

HOW IS CETROTIDE/ORGALUTRAN ADMINISTERED?

Cetrotide/Orgalutran are given as a subcutaneous (under the skin) injections.

ARE THERE ANY SIDE EFFECTS ASSOCIATED WITH CETROTIDE/ ORGALUTRAN?

Because it acts quickly and directly, Cetrotide/Orgalutran is generally well tolerated. Mild and short-lasting reactions, like reddening, itching, and swelling, may occur at the injection site. Some patients also experience nausea and headache. Consult your doctor if you experience these or any other side effects.

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Orgalutran: How to use Orgalutran

Treatment with Orgalutran should be started under the supervision of a fertility specialist. Orgalutran is given as a subcutaneous (under the skin) injection in the thigh or stomach. The injection site should be changed every day to lessen possible injection site reactions. If your doctor or nurse decides you can give the injections yourself, they will teach you the injection technique.

Do not attempt self-injection until you are sure of how to do it. Follow all instructions given to you by your doctor or nurse carefully.

How much to inject

The usual dose is the contents of one pre-filled syringe of Orgalutran once a day on specific days of the menstrual cycle. Your doctor will tell you when to inject Orgalutran.

How to use Orgalutran

Follow these steps:

1. Prepare the injection site

Orgalutran® (or- GAL-u-tran) Wash your hands thoroughly with soap and water. Swab the injection site with a disinfectant, on an area about 5 cm around the site. Let the disinfectant dry for at least one minute before proceeding.

2. Open the outer pack and plastic container inside

While waiting for the disinfectant to dry, open the Orgalutran pack and remove the plastic container. Carefully open the plastic container and remove the Orgalutran syringe. You will see the needle is already attached, covered by a grey needle shield.

3. Prepare the syringe for injection

Remove needle shield and discard it in a sharps-disposable bin. Hold the syringe with the needle facing upwards and push the plunger a little if needed to expel any air. You are now ready to inject Orgalutran. I suggest not priming (ie expelling air) as it sometimes leads to loss of fluid.

4. Inserting the needle and injecting

Orgalutran is injected in either the thigh or the abdomen, usually near the navel. Pinch up a large bit of skin between your finger and thumb. Insert the needle at the base of the pinched-up skin at an angle of 45 to 90 degrees to the skin surface. Gently draw back on the plunger to see if the needle is inserted correctly. If blood appears, the needle is not inserted correctly so do not inject the Orgalutran.(this is not usually necessary with a subcutaneous injection) Remove the needle, cover the injection site with a sterile swab and dispose of the syringe in a sharps-disposable container. Start again with a new syringe. If the needle has been inserted correctly, depress the plunger slowly and steadily until all the solution has been injected.

Vary the different injection site each time to minimise local irritation.

5. Removing the needle

Pull the needle out of the skin quickly and apply pressure to the site with a swab containing disinfectant. Dispose of the syringe (with the attached needle) in a Sharps Container. Use the syringe only once and then dispose of it in the Sharps Container.

How long to use Orgalutran Your doctor will tell you when to inject Orgalutran and when to stop injecting it.

If you forget to use Orgalutran

If you forget an injection, contact your doctor or IVF clinic immediately for advice.

Do not inject a double-dose to make up for the forgotten dose.

If you inject too much

Immediately contact your doctor or IVF clinic

Storage

Keep Orgalutran in a safe place away from the sight and reach of children.

A cupboard at least one-and-a-half-metres above the ground is a good place to store medicines.

Keep Orgalutran below 30°C. Do not put it in the freezer as the syringe may break.

Keep the syringe in the outer carton to protect it from light (keep in fridge for ease).

Disposal

Dispose of your Orgalutran syringe and needle safely into a yellow plastic Sharps Container.

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Cetrotide

Cetrotide® blocks the effects of a natural hormone, called gonadotropin-releasing hormone (GnRH). GnRH controls the secretion of another hormone, called luteinizing hormone (LH), which induces ovulation during the menstrual cycle. During hormone treatment for ovarian stimulation, premature ovulation may lead to eggs that are not suitable for fertilization. Cetrotide® blocks such undesirable premature ovulation.

Uses

Cetrotide® is used to prevent premature ovulation during controlled ovarian stimulation.

General Cautions

Do not use Cetrotide® if you

- have kidney disease
- are allergic to cetrotirelix acetate, mannitol or exogenous peptide hormones (medicines similar to Cetrotide®) or
- are pregnant, or think that you might be pregnant, or if you are breast-feeding. Consult your doctor before taking Cetrotide® if you have had severe allergic reactions.

Proper Use

Ovarian stimulation therapy is started on cycle Day 2 or 3. Cetrotide® is injected under the skin either once daily (0.25 mg dose) or once (3 mg dose), as directed by your physician. When an ultrasound examination shows that you are ready, another drug (hCG) is injected to induce ovulation.

How should you use Cetrotide®?

You may self-inject Cetrotide® after special instruction from your doctor.

To fully benefit from Cetrotide®, please read carefully and follow the instructions given below, unless your doctor advises you otherwise.

Cetrotide® is for injection under the skin of the lower abdominal area, preferably around, but staying at least one inch away from the belly button. If you are on a multiple dose (0.25 mg) regimen, choose a different injection site each day to minimize local irritation. Dissolve Cetrotide® powder only with the water contained in the pre-filled syringe. Do not use a Cetrotide® solution if it contains particles or if it is not clear.

Before you inject Cetrotide® yourself, please read the following instructions carefully:

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Directions for using Cetrotide® 0.25 mg or 3 mg with the enclosed needles and pre-filled syringe:

1. Wash your hands thoroughly with soap and water.
2. On a clean flat surface, lay out everything you need (one vial of powder, one pre-filled syringe, one injection needle with a yellow mark, one injection needle with a grey mark, and two alcohol wipes).
3. Flip off the plastic cover of the vial. Wipe the aluminum ring and the rubber stopper with an alcohol wipe.
4. Take the injection needle with the yellow mark and remove the wrapping. Take the pre-filled syringe and remove the cover. Twist the needle on the syringe and remove the cover of the needle.
5. Push the needle through the center of the rubber stopper of the vial. Inject the water into the vial by slowly pushing down on the plunger of the syringe.
6. Leave the syringe in the vial. Gently shake the vial until the solution is clear and without residue. Avoid forming bubbles during dissolution.
7. Draw the total contents of the vial into the syringe. If liquid is left in the vial, invert the vial, pull back the needle until the opening of the needle is just inside the stopper. If you look from the side through the gap in the stopper, you can control the movement of the needle and the liquid. It is important to withdraw the entire contents of the vial.
8. Detach the syringe from the needle and lay down the syringe. Take the injection needle with the grey mark and remove its wrapping. Twist the needle on the syringe and remove the cover of the needle.
9. Invert the syringe and push the plunger until all air bubbles have been pushed out. Do not touch the needle or allow the needle to touch any surface.
10. Choose an injection site in the lower abdominal area, preferably around, but at least one inch away from the belly button. If you are on a multiple dose (0.25 mg) regimen, choose a different injection site each day to minimize local irritation.

Take the second alcohol wipe and clean the skin at the injection site and allow alcohol to dry. Inject the prescribed dose as directed by your doctor, nurse or pharmacist.

11. Use the syringe and needles only once. Dispose of the syringe and needles immediately after use (put the covers on the needles to avoid injury). A medical waste container should be used for disposal.

Directions for using Cetrotide® 0.25 mg with the Serono Fertility Auto-injector™:

1. Follow Steps 1-5 above for enclosed needles and syringe.
2. Remove the empty syringe from the vial and discard. Gently swirl the vial until the solution is clear and without residues. Avoid forming bubbles during dissolution.
3. Insert the 1 mL fixed needle syringe (provided for use with the Serono Fertility Auto-injector™) through the center of the rubber stopper of the vial. Keeping the needle in the vial, lift the vial and turn it upside down with the needle pointing toward the ceiling. With the needle tip in the liquid, draw the total contents of the vial into the syringe. If liquid is left in the vial, invert the vial and pull back the needle until the opening of the needle is just inside the stopper. If you look through the side through the gap in the stopper, you can control the movement of the needle and the liquid. It is important to withdraw the entire contents of the vial. Remove the needle from the vial.
4. Proceed to Instructions for Use provided with the Serono Fertility Auto-injector™ for use with a 1 mL fixed needle syringe.

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SPECIAL ADVICE

What do you do if you have used too much Cetrotide®?

Contact your doctor in case of overdosage immediately to check whether an adjustment of the further ovarian stimulation procedure is required.

Possible Side Effects

Mild and short lasting reactions may occur at the injection site like reddening, itching, and swelling. Nausea and headache have also been reported.

Call your doctor if you have any side effect not mentioned in this leaflet or if you are unsure about the effect of this medicine.

Storage

How is Cetrotide® to be stored?

Store Cetrotide® in a cool dry place protected from excess moisture and heat. Store Cetrotide® 3 mg at 25°C (77°F). Excursions are permitted to 15-30°C (59-86°F). Store Cetrotide® 0.25 mg in the refrigerator at 2-8°C (36-46°F). Keep the packaged tray in the outer carton in order to protect it from light.

How long may Cetrotide® be stored?

Do not use the Cetrotide® powder or the pre-filled syringe after the expiration date, which is printed on the labels and on the carton, and dispose of the vial and the syringe properly.

How long can you keep Cetrotide® after preparation of the solution?

The solution should be used immediately after preparation.

Store the medicine out of the reach of children.

If you suspect that you may have taken more than the prescribed dose of this medicine, contact your doctor immediately. This medicine was prescribed for your particular condition. Do not use it for another condition or give the drug to others.

This leaflet provides a summary of the information about Cetrotide®. Medicines are sometimes prescribed for uses other than those listed in the Leaflet. If you have any questions or concerns, or want more information about Cetrotide®, contact your doctor or pharmacist.