

INTRAUTERINE INSEMINATION (IUI)

Intrauterine insemination is a fertility enhancing procedure in which sperm are washed, concentrated, and injected directly into a woman's uterus through the vagina. During natural intercourse, only a fraction of the sperm make it up the woman's genital tract. Intrauterine insemination increases the number of sperm in the uterus and fallopian tubes – where fertilization takes place. Intrauterine insemination is most successful when it is used along with certain fertility drugs to enhance ovulation. There are a number of different fertility drugs that are available. Some of these drugs can be taken orally – others need to be given by injection. The costs of these drugs, success rates and side effects are very variable and specific. This technique is often called controlled ovarian hyperstimulation and IUI (COH/IUI) or superovulation/IUI.

CANDIDATES:

Superovulation and IUI is often recommended for couples with no known cause of infertility who have been trying to have a baby for at least a year. It may be considered sooner than a year in an older woman. You should have thorough infertility investigations before trying this procedure. Under normal circumstances, IUI uses sperm from your male partner. If you do not have a partner, or if your partner has very poor quality sperm, then therapeutic donor insemination using screened sperm samples from anonymous donors would be considered.

MALE PARTNER REQUIREMENTS:

Studies suggest that IUI will not be effective in cases where the male has very low sperm counts or poor sperm quality. Therefore, before proceeding with this process, sperm tests need to show reasonable sperm function.

FEMALE PARTNER REQUIREMENTS:

Tests will need to be done to confirm regular ovulation, normal uterine cavity, patent fallopian tubes, and normal hormone levels. In certain circumstances, if history and examination suggest possible pelvic pathology, a laparoscopy might be recommended. Laparoscopy is an operative procedure done under general anesthetic. This involves putting a small telescope through the belly-button to further evaluate the pelvic organs (uterus, fallopian tubes and ovaries).

SUCCESS RATES:

The success rates of superovulation with intrauterine insemination depend on a number of factors. Maternal age and the quality of the male partner sperm count are the most important.

RISKS OF SUPEROVULATION/IUI:

1. Infection. Whenever something is injected in to your body there may be a risk of infection – although this risk is very small. However – if after an IUI you experience increasing abdominal pain, fever, smelly discharge or burning when passing urine – you should contact VFC right away and request an urgent assessment. It is common to have some discomfort after ovulation/IUI – especially if you have more than 1 follicle (egg)
2. The fertility drugs that are used to stimulate the ovaries increase the risk of multiple pregnancy and ovarian hyperstimulation syndrome. There will be further information on these subjects in this handout.

PROCEDURES:

1. **Drug treatment.** There are a number of different fertility enhancing drugs (ovulation induction agents) available. They may be used alone or in combination with each other. The most commonly used drugs are Clomiphene pills, Letrozole pills or gonadotropin injections.

Clomiphene or Letrozole pills are given usually for five days, starting on the third day of the cycle. Gonadotropin injections are considerably more expensive, though also more successful, and are usually given on a daily basis, starting at around Day 3 to 5 of your cycle. Injectable drugs include Puregon, Gonal F, Repronex and Bravelle. Another medication that may be prescribed is called HCG. HCG is a hormone that has a similar structure to LH and is used to trigger ovulation. It also helps smaller follicles/eggs mature – and does result in extra support to the lining of the uterus (endometrium) after ovulation

2. **Monitoring treatment.** This is done to measure the growth of the follicles, individualize drug doses and prevent serious side effects. Normally speaking an ultrasound will be done in the office on either the first, second or third day of your period, before you start the treatment. This will allow evaluation of your ovaries before they are stimulated. The days of your cycle are always counted using the first day of your period as Day 1. After the baseline ultrasound, you will start using the fertility drugs prescribed. On approximately Day 10 - 12, (or sooner if you have been prescribed injectable medications) you will be asked to return to the office for another ultrasound. The eggs grow on the ovaries in capsules of fluid called follicles. These are easily monitored by ultrasound. Ultrasound is done to determine the number and size of the follicles developing.

Ultrasound image of developing follicles



Depending on the ultrasound result, you may be asked to have a blood test to check estrogen levels. The dosage of your drugs may be adjusted depending on the response. The usual aim for this process is to generate three to five mature follicles. Depending on what drugs are used, an egg is normally mature once the follicle reaches a size of 16 – 22 mm.

3. After Day 9 or 10 you may be asked to monitor your urine daily using an ovulation predictor kit . There is further information on monitoring for this later on in this handout. Occasionally the brain will trigger ovulation (called an LH surge) before all the follicles are ready. We need to be aware of this.
4. When enough follicles have reached their target size, you will be given an injection of a hormone to induce ovulation. This drug is called HCG
5. Ovulation will occur 24-36 hours after the ovulation inducing injection. On that day, your partner will be asked to produce a specimen of semen by masturbation into a sterile container. It is preferable if the semen sample is produced on site at VFC. This fresh semen will then be

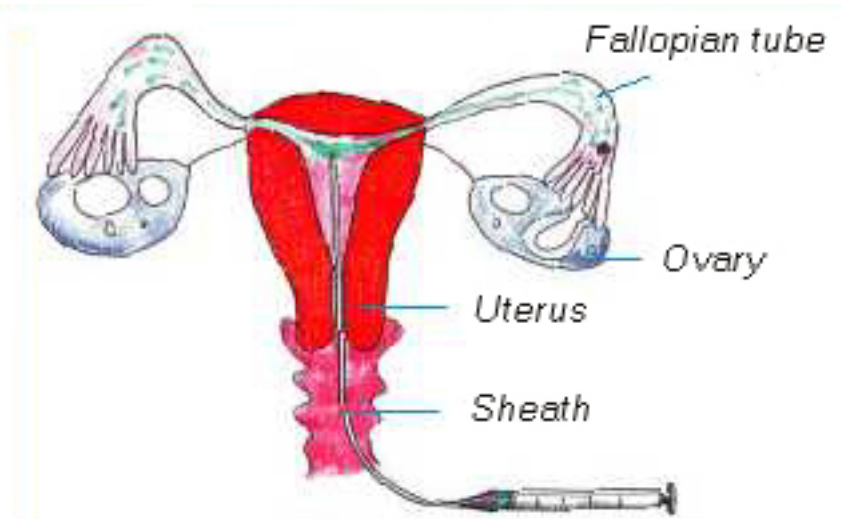
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washed and concentrated, a process which takes approximately one to two hours. Using a fine catheter, the sperm concentrate will then be injected through the cervix into the uterus. The procedure is fairly painless, though on occasion may cause some mild to moderate discomfort. After the insemination you will be asked to lie quietly in the office for at least 10 minutes

Intercourse over the next few days is also encouraged. It is then life as usual – although we suggest you avoid excessive exercise for the week following the IUI. Light exercise is fine.



You will be asked to have a pregnancy test (blood test) 2 weeks after the IUI. Even if you feel you are not pregnant and experience bleeding – we please request that you still have the pregnancy test done – to make sure that you do not have an ectopic pregnancy or other pregnancy related complication. If you have this test done first thing in the morning we will usually have the result by the afternoon and will try and call you with the result. If you have not heard from the clinic by the following morning please call VFC.

DRUG COSTS:

1. Letrozole. The cost is about \$40.00 for a cycle.
2. Clomiphene. The cost of a cycle of Clomiphene is approximately \$80.00.
3. Drug to trigger ovulation. The drug that is used to induce ovulation contains a hormone called HCG. The cost is about \$85.00 - \$90.00
4. Gonadotropin costs.(Gonal F,Puregon,Repronex) Gonadotropins are drugs that are used to directly stimulate the ovaries. They need to be given by injection on a daily basis. They are expensive, and the total cost of a cycle would depend on the number of ampoules required. On average, the drug costs will be anywhere between \$500.00 and \$1500.00 per cycle.
5. The costs of sperm washing. This covers a presperm count and assessment, the sperm wash itself, post wash count and assessment, the preparation of the sperm for insemination and the intrauterine catheter.Please refer to the VFC fee schedule for updated costs – however it is in the region of \$350.00

Success rates are very dependent on a number of factors which include but are not limited to:

A woman's age
 Her FSH level
 The sperm quality
 The length of time you have been trying to get pregnant
 The status of the fallopian tubes
 The presence of endometriosis or pelvic adhesions (scar tissue)

An approximation of the pregnancy rates per cycle of superovulation/IUI performed for the correct indications are as follows:

1. 20% for women under the age of 30.
2. 15 % - 18% for women aged between 30 and 35.
3. 10 - 15% for women aged 35 to 39.
4. 5 - 10% for women over the age of 40.

However, the projected success rates really need to be individualized. It does depend largely on age and the choice of medication. Using gonadotropins improves pregnancy rates over using an oral agent like clomiphene. For instance, in the couple under the age of 30 with normal sperm parameters and using gonadotropins to stimulate ovulation, the success rate may be as high as 25% per cycle. At the other extreme, in the woman who is over 40, using only Clomiphene to stimulate the ovaries, the success rate for ovulation induction with Clomiphene and IUI might only be about 2 – 5 % per cycle.

When considering the success rates of fertility treatments – it is important to remember that 100 % does not exist.

The chances for a successful pregnancy in a healthy fertile woman with a fertile partner is age dependent and is listed below:

Age of female	Chance of pregnancy per cycle	Chance of Miscarriage
Under 30 years	25 %	10 %
Age 35 years	15 %	18 %
Age 40 years	5 – 10 %	25 %
Age 45 years	1-2 %	90 %

Ovulation predictor testing

Normal Menstrual cycle

During a normal menstrual cycle a woman will usually ovulate just once. Ovulation is controlled by the pituitary gland in the brain.

Eggs grow in the ovaries – in little capsules of fluid called follicles. A follicle is therefore a small cyst which contains an egg. As the follicle grows – the egg matures. During this process the follicle releases a hormone called estrogen. The pituitary gland in the brain monitors the levels of estrogen. When the estrogen level reaches a certain threshold – the brain realizes that the egg is mature. At this stage the pituitary gland in the brain “triggers” ovulation.

The pituitary gland in the brain does this by releasing a hormone called LH (luteinizing hormone) LH triggers ovulation. This is called an **LH surge**

The LH surge causes the ovary to release an egg (ovulation) about 24 – 36 hours later. We are able to detect the presence of this LH in your urine by using an LH predictor kit.

So by testing your urine every day, we are able to predict when you are going to ovulate.

There are a number of Ovulation predictor kits available. Kits which are readily available at most pharmacies include First Response, Clearplan, Ovuquick etc.

Some of these kits can be quite expensive. You can also order Ovulation predictor kits very cheaply on line from www.saveontests.com. I suggest you buy the cassettes rather than the strips.

Ovulation will normally occur about 14 days before your next period. So if you have a 28 day cycle – you should ovulate around day 14. This would mean that you would have an LH surge on day 13. If you have a 24 day cycle – we would expect you to ovulate around day 10. This would mean that you would have an LH surge on Day 9.

In order to detect Ovulation – you should start testing your urine at least 2 days before you expect to have an LH surge. For most people – if you start testing on about day 10 or 11 you will not miss the surge.

Instructions for testing.

It is always best to test at about midday. Please follow the instructions below.

1. After breakfast – please empty your bladder and do not have anything further to drink until you do your test. This will allow your urine to be concentrated and avoid the risk of “missing” the LH surge due to dilute urine.
2. Empty your bladder again at about 10 am.
3. At around midday test your urine – having not voided for at least 2 hours.
4. Follow the instructions from the test kit

The instructions will tell you that your test is positive if your surge line is as dark as the Reference line.

For patients who are planning an IUI (intrauterine insemination) using their partners sperm, or for those patients planning an IUI with donor sperm (DI) – please follow the instructions below.

If your test line is nearly as dark as the reference line – it means that you are starting to have an LH surge – and you should contact VFC.

If your surge is on a weekday – please call VFC between 1 – 3 pm, and book your IUI for the following day.

WEEKENDS – IMPORTANT

For testing on weekends – please note that we only work mornings. It is important that you do your test before midday – and be sure to notify us BEFORE midday that you have had a surge. Please first try calling VFC at 704 0024 or 704 0015. If there is no reply – then please call our clinical co ordinator or Dr.Hudson at the following numbers.

Clinical co ordinator	250 889 0526
Dr.Hudson	Cell 250 704 6653 OR Home 250 472 3432

We will then get particulars for you and arrange for the IUI the following day.

IMPORTANT: Over weekends, if you do not inform of us of your surge by midday, we will likely NOT be able to accommodate you the following day.

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The Risk of Multiple Pregnancies

The term “multiple pregnancy” refers to a pregnancy that includes more than 1 fetus (baby) Most multiple pregnancies are twins. However higher order multiple pregnancies such as triplets and quadruplets can also occur.

The incidence of naturally occurring twins in the general population is about 1 in 80. There does tend to be a familial risk – in that if you have a family history of twins, your risk may be higher. The risk of naturally occurring triplets is about $1/80$ squared = $1/6400$. The risk of naturally occurring quads is $1/80$ to the power of 3 = $1/512,000$.

However – the risk of multiple pregnancies is significantly increased with the use of fertility treatments. The risk with fertility drugs which induce ovulation (i.e. stimulate the ovaries to release more than 1 egg) of inducing a multiple pregnancy may be related to a number of factors. These include maternal age, the number of eggs being released (this is something that can be monitored by ultrasound), the quality of the sperm (i.e. the chances of sperm fertilizing the eggs) the length of fertility difficulties, etc.

Generally speaking there are 3 forms of fertility treatments which may put you at risk for a multiple pregnancy.

1. The use of fertility drugs (such as Clomiphene, Femara, and injectable drugs) to induce ovulation.
2. The use of fertility drugs to induce ovulation – combined with intra uterine insemination. (IUI)
3. In Vitro Fertilization. Here the risk is directly related to the number of embryos that are transferred in to the uterus.

There are many risks related to multiple pregnancies, and obviously the risks are increased with higher order multiple pregnancies e.g another more than twins.

These risks are divided in to 2 groups....

1. Risks to the mother. Any complication that can occur in pregnancy may do so more often when there is a multiple pregnancy. For example.....these include but are not limited to the following.....
 - a. Anemia
 - b. Miscarriage
 - c. Diabetes
 - d. Toxemia (high blood pressure)
 - e. Fatigue, nausea and vomiting

- f. Excessive weight gain and fluid retention
 - g. Premature labour
 - h. Hospitalization
 - i. Need for time off work
 - j. Thyroid dysfunction
 - k. Blood clots – thrombo embolism
 - l. C section
 - m. Post partum bleeding (hemorrhage)
 - n. Post partum depression
 - o. Social stress – dealing with 2 babies
2. Risks to the babies. The main risk here is of premature delivery and low birth weight. Such risks include but are not limited to
- a. Intra uterine growth restriction_(i.e. poor growth in utero)
 - b. Congenital abnormalities e.g. club foot, cleft palate etc. The overall risk to any fetus of having some form of abnormality is about 3 – 4 %, but this risk appears to be slightly higher with multiples.
 - c. Chromosome abnormalities. As women get older the risk of having a child with some form of Chromosome problem (such as Downs syndrome) is higher. The risk is slightly increased with twins, triplets etc.
 - d. Premature delivery and low birth weight.
 - e. Low birth weight can then be associated with learning difficulties, attention deficit disorder, poor growth after birth etc.
 - f. Cerebral palsy – the risk of a twin having CP is about 5 - 10 X that of a singleton baby. (On average the risk of cerebral palsy in singleton babies is about 1 – 2/1000, in twins is about 5 – 10/1000 and in triplets is about 30/1000.

Due to the quality of peri natal care today, the chances for babies surviving if they are born prematurely (after 25 weeks gestation) is high – but the risk of long term complications increases the earlier they are delivered and the lower the birth weights.

In our attempts to help couples to overcome infertility and get pregnant – with the use of fertility drugs, IUI and IVF – there will be an increased risk of multiple pregnancy. We at VFC do everything we can to maximize your chance of getting pregnant and reduce the chance of multiple pregnancy.

If a multiple pregnancy was to occur, and if there were more than twins, one option to improve the outcome for both mother and babies is a selective reduction. This is a procedure whereby one or more of the fetuses is “sacrificed”. It is like having a selective abortion so that the number of fetuses in utero is reduced. It is usually done at about 11 – 12 weeks gestation by a procedure similar to an amniocentesis. It is a difficult thing to go through – and apart from the emotional distress, can also cause a risk of miscarriage. i.e. the procedure itself may risk the entire pregnancy being miscarried. The risk of losing the entire pregnancy from a selective reduction is about 5 – 6 %.

The risks related to triplets and more – for Mother and babies – is extremely high. In most cases if this occurs it will be recommended that you consider a selective reduction. Please feel free to discuss this further with Dr.Hudson before following through with any treatment regimen.

This form MUST be signed and handed in the VFC before proceeding with treatment.

Acknowledgement form: Risks of multiple pregnancy

I hereby acknowledge that I have read the information provided me about the risks of multiple pregnancy. I am aware that the medication prescribed and treatment advocated at the Victoria Fertility Center may increase the risk of my having a multiple pregnancy.

I have had an opportunity to discuss these issues with the medical staff at the Victoria Fertility Center and feel well informed of my options

Date: _____

Name: _____

Signed: _____

Name of Partner _____

Signed: _____

This form should be either personally handed in to VFC or faxed to VFC at 250 704 0034.

Clomiphene

(also known as Serophene or Clomid)

Clomiphene is a fertility medication used for the following purposes.

1. To induce ovulation in a woman who is not ovulating normally. There can be a variety of reasons why a woman may not ovulate. One of the most common of these is polycystic ovarian syndrome. (PCOS) More can be read about PCOS on our website. (www.Victoriafertility.com)
2. As a first-line fertility drug in women who may be ovulatory but are experiencing problems with fertility. The medication in this instance may be prescribed to try and coax the ovaries to release more than one egg and thereby enhance fertility. In this instance it is often given along with a treatment called intrauterine insemination.(IUI)

How is this medication prescribed

Clomiphene comes in 50 mg tablets. The normal starting dose would be either 1 or 2 tablets (50 – 100 mg) taken every day for 5 days, starting on day 3 of the menstrual cycle. (day 1 is the first day of menstrual flow)

The response to clomiphene is very variable depending on a woman's age, weight and ovarian reserve. In some cases the response expected or hoped for may be less or more than actually occurs. For this reason it may be recommended that your ovaries are monitored by ultrasound to see exactly what response occurs. Although eggs are microscopic they grow in little capsules of fluid called follicles which are easily monitored by ultrasound

Side effects

Side effects are quite common and occur in at least 50% of patients who take clomiphene.

Side effects include the following:

1. abdominal bloating
2. pelvic discomfort
3. nausea
4. fatigue
5. breast discomfort
6. moodiness and irritability
7. visual disturbances
8. depression
9. lightheadedness or dizziness
10. Hot flashes and night sweats
11. Hepatitis (extremely rare)

Risks

There is a very small risk of ovarian hyperstimulation syndrome. Personally I have never ever seen OHSS occur with clomiphene alone.

One of the most significant risks that every patient taking clomiphene should be aware of is of multiple pregnancy.

Many patients who are prescribed Clomiphene at Victoria Fertility Center will have their ovaries monitored by ultrasound. You will therefore be informed of how many eggs will be releasing so will have a more definite idea of the risk of multiple pregnancy.

If you have any further questions about this you should speak to Dr. Hudson or one of the health care professionals at Victoria Fertility Center

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The Use of Femara (Letrozole) for Infertility

Femara was first reported to be effective for ovulation induction by Dr. Casper in Toronto in the late 1990s

In October of 2005, a group from Quebec reported on 150 pregnancies born as a result of Femara or Femara and injectable fertility medications. They found that the babies were born with a significantly **lower birth weight** than a control group of babies delivered in the same hospital. They also found that **the congenital abnormality rate was not different but that congenital abnormalities of the limbs and cardiovascular system were over-represented in the group using Femara.**

On November 17, 2005, Novartis, the company that makes Femara issued a contraindication for the use of Femara in women with premenopausal endocrine status (therefore women who might use it for infertility treatment), in pregnancy, and/or lactation due to the potential for maternal and fetal toxicity and fetal malformations.

The Evidence

The evidence against Femara came in an oral presentation from which we have included the whole abstract just to the right. There are several important things to point out about the abstract.

First and most importantly, the article **does not demonstrate an increased abnormality rate in the Femara group compared to the control group.** The baseline congenital abnormality rate we expect in all births independent of how the pregnancies were conceived is about 3%. We would therefore expect 4 or 5 congenital abnormalities in 150 babies.

The Outcome of 150 Babies Following the Treatment with Letrozole or

Letrozole and Gonadotropins. M. M. Biljan, R. Hemmings, N. Brassard. Montreal Fertility Centre, Montreal, PQ, Canada; St. Mary's Hospital, Montreal, PQ, Canada; Universite' Laval, Quebec, PQ, Canada.

OBJECTIVE: Letrozole is a medication widely used for secondary breast cancer prevention. Recently, this aromatase inhibitor has been used for ovulation induction. In this analysis we report the outcome of 150 babies born as a result of treatment with either letrozole alone or a combination of letrozole and gonadotropins at the Montreal Fertility Centre.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: This analysis includes patients with unexplained infertility and patients with polycystic ovarian disease. As a control group we used patients delivered at "St. Mary's" hospital in Montreal between 1995 and 2004. The choice of the hospital was deliberate, as "St. Mary's" hospital delivers mostly low risk babies.

RESULTS: During a period of 25 months 171 babies were born as a result of the use of letrozole or letrozole and gonadotropins. Twenty one babies were lost for follow-up. One hundred and fifty babies were compared with a data-base of normal deliveries containing 36,050 deliveries. The median age (M) of treated patients was 35.2 years (interquartile difference(IQD)_ 31.4-37.9). We had 110 singleton and 20 twin pregnancies. All twin pregnancies apart of one were conceived following the treatment with letrozole and gonadotropins. The incidence of vaginal bleeding was 36.7% in the first trimester, 7.3% in the second trimester, and 1.3% in the third trimester. Seventy-seven non-diabetic singleton pregnancies were delivered

at term. There was no difference in weight between this group and the control. Twenty patients had gestational diabetes. Seventeen patients with gestational diabetes delivered at term. When compared with controls these babies were of a significantly lower birth weight than controls (p_0.002 95%CI_11.3-136.6). **Incidence of all malformations was not different between the two groups** (p_0.25 95%CI_0.78-4.71). However, the incidence of locomotor malformations (p_0.0005 95%CI_2.64-27.0) and cardiac anomalies (p_0.0006 95%CI_3.30-58.1) was higher than in the control groups.

CONCLUSION: The results of this study show that use of letrozole in ovulation induction should be controlled until more data on outcomes of pregnancies is obtained.

This is exactly what was found!

The second thing to point out about the article is that they did find a **significantly lower birth weight in the Femara pregnancy group** than the control group. At first this may appear like another bad side effect of Femara. However, Femara has a half life of 44 hours. The half life of a drug is the time it takes the body to eliminate half of the drug. It is difficult to understand how a drug that would be gone from the body by the time implantation occurs could cause a difference in the birth weight almost nine months later. A more feasible explanation for this is that there was something else different between the control group that was used and the Femara pregnancy group.

Notice that the **control group was “the babies delivered at St. Mary’s Hospital between 1995 and 2004**. These were not infertility patients. The article goes on to say that the age of the infertility patients was 35.2 years. The average age of women having babies in Canada in 1999 was 29.1 years old. Therefore the femara group was likely older. Twenty of the 130 pregnancies were twins. This is a rate of just over 15% compared to 1.25% in the general population. The article goes on to describe the incidence of vaginal bleeding in all three trimesters. The numbers are not compared to the control population but these numbers do appear very high. Twenty (15.4%) of the Femara pregnancies were complicated by gestational diabetes. This is a higher number than would be expected in the whole population.

Therefore the **Femara pregnancy group differed from the control group** in that they were older, had more bleeding during their pregnancies, more twins and more gestational diabetes. These differences or something else different about the control group is probably a more likely explanation for the higher birth weight in this group. These differences might be more likely to explain a higher congenital abnormality rate than the use of Femara but remember, there wasn’t a higher abnormality rate!

The control group differed in **one more important way** from the Femara pregnancy group. There were 130 pregnancies in the Femara group and 36,050 in the control group. Remember that the main concern from this article was that some congenital abnormalities (limb and cardiac) were over represented in the Femara pregnancy group. This may only be an artifact of the difference in sample sizes. The control group is 277 times as large. Congenital abnormalities are rare (3% of pregnancies). Specific congenital abnormalities are even rarer, perhaps less than one in 1300. I picked 1300 not because that is the rate of specific abnormalities but to help me make this point.

If a rare congenital abnormality (1/1300) happens in a small study group like the Femara pregnancy group (1/130) its frequency automatically appears 10 X as great. Several medications which have later proven to be safe have been caught in this trap. Clomiphene citrate and Diclectin both had articles written early in their use that suggested over-representation of specific congenital abnormalities. Both have gone on to be demonstrated safe by over 50 clinical studies each.

The Contraindication

As a result of the article discussed above, Novartis, the company that makes Femara issued a notice which was dated November 17, 2005 and mailed to physicians. This announced a “Health Canada Endorsed Important Safety Information on Femara”. The notice went on to say that Femara is contraindicated in women with premenopausal endocrine status, in pregnancy, and/or lactation due to the potential for maternal and fetal toxicity and fetal malformations. Women with premenopausal endocrine status would include anyone trying to become pregnant.

The contraindication is not new. It was included in the product monograph on Femara dated March 22, 2004. Novartis, like other pharmaceutical companies is committed to the safe use of its medications. Also, a formal notice re-stating the contraindication is good public relations and certainly a safety precaution against any potential law suits that could result from pregnancies complicated by congenital abnormalities.

The Use of Femara at Dr.Casper's Fertility Clinic in Toronto (TCART- Toronto Centre for Advanced Reproductive Technology))

As stated earlier, Femara has been used extensively for many years at TCART. TCART keeps very close tabs on its successful pregnancies. Since the presentation of the Montreal abstract, they have published a multicentre trial of 911 babies born after letrozole or clomiphene citrate treatment in a prestigious journal called Fertility and Sterility. They found no increase in congenital anomalies in the Femara (Letrozole) babies, and in fact, observed a significant reduction in heart defects in the letrozole babies compared to the babies born after their mothers were given clomiphene.

Initially they found that some women who would **not ovulate on clomiphene citrate** would respond to Femara and that the pregnancy rate using Femara was twice as high as clomiphene citrate.

They presented their first 100 pregnancies using Femara and intrauterine insemination in 2005. In this presentation, they demonstrated a **twinning rate** of about 4% of Femara conceptions compared to over 20% with clomiphene citrate. Therefore low dose Femara is often used when it is important to avoid a multiple pregnancy.

What Should Femara Users Do ?

Some clinics have decided to discontinue the use of Femara .

At VFC, **we ask you to make an informed decision** if you wish to use Femara or another aromatase inhibitor called Arimidex. Arimidex is being studied in a current FDA-approved phase 2 clinical trial in the United States for use as an ovulation induction agent, based on the original research with Femara. To use either Femara or Arimidex, we must know and document that you have made this decision after weighing all the available evidence. You must know that the number of pregnancies resulting from Femara is too few to give absolute reassurance that it is safe. I would like you to have read this information sheet and our recent publication in Fertility and Sterility which is attached.

I have provided this information sheet to inform you and help you make your decision. If you have additional questions, we will try and answer them. I will let you know more as the evidence unfolds.

Personally we find that success rates with Letrozole are higher than with clomiphene and have not noticed an increased risk of birth defects at VFC

Consent to use Letrozole (Femara)

If after reading this information sheet and researching any other resource, you would like to continue Femara, please fill in the following and give it to one of our VFC. staff

I, _____, have read the information sheet on “The Use of Femara for Infertility”. I understand that there may be some risks and that sufficient data does not exist to completely reassure that it does not cause congenital abnormalities. I also understand that an alternative treatment plan will be devised for me if I wish not to use this product.

I have chosen to continue to use Femara and understand the fact sheet I have been given.

Printed Name: _____

Signed _____

Date : _____

This form must be signed and either delivered to VFC or faxed in before you use this medication.

VFC Fax number: 250 704 0034