

CONSENT FORM FOR TREATMENT WITH OVULATION INDUCTION MEDICATIONS AND INTRAUTERINE INSEMINATIONS

INSTRUCTIONS:

This consent form provides a description of the treatment that you are undertaking.

- Read the consent completely. If you have any questions please speak with your doctor.
- Do not make any additions or deletions to the consent.
- Treatment **cannot** be started until all consents are signed.
- Consents must be signed in front of your nurse or physician.

INTRODUCTION

Ovulation induction medications can help an infertile patient achieve a pregnancy by stimulating the ovulation of eggs from the ovaries. Ovulation inducing medications are often used in conjunction with intrauterine inseminations. Sometimes intrauterine inseminations are used without any preceding medications. This document explains ovulation inducing medications and intrauterine insemination treatment.

This consent is valid for a period of one calendar year after it has been signed. Please make a copy for your records. It is recommended that you review the consent prior to each treatment cycle. If you have any questions about your treatment then it is your responsibility to speak with your physician.

Pre-treatment Recommendations:

During treatment the patient should avoid any activity, behavior and medications that could reduce her chance of conceiving and having a healthy baby. In addition, the recommendations listed below should be followed.

1. A prenatal vitamin should be taken on a daily basis before the treatment is begun. This will reduce the chance that a baby will be born with a neural tube defect (e.g. spina bifida), which is a birth defect that effects the development of the spine.
2. Smoking must be avoided before and during treatment. It is also contraindicated during pregnancy.
3. Recreational drugs are absolutely contraindicated.
4. Ingestion of aspirin or aspirin-like products (e.g. Motrin[®], Advil[®], Anaprox[®], Naprosyn[®], Aleve[®], etc.) should be avoided during treatment. However, in certain circumstances your doctor may prescribe low dose aspirin (baby aspirin, 81 mg). Tylenol[®] is safe to take before and during pregnancy.
5. The use of alcohol should be avoided during treatment and after pregnancy is established.
6. The use of all prescription and over-the-counter medications (including herbal remedies) should be discussed with a physician before starting a treatment cycle.
7. HIV (human immunodeficiency virus) screening is strongly recommended for all couples undergoing infertility treatment. HIV is the virus that causes acquired immunodeficiency syndrome (AIDS). A

patient infected with HIV can pass the virus to her unborn child. Please talk to your physician about having this test performed.

8. Ingestion of some fish, which contain higher amounts of mercury, can affect the development of the nervous system of a fetus. During the treatment and after pregnancy is established you should avoid eating these fish- shark, swordfish, king mackerel, tilefish and canned tuna fish. You should limit the intake of all other fish to 12 oz. per week.

DESCRIPTION OF TREATMENT

This treatment involves several steps as outlined below. Patients are not guaranteed success at any or all of these steps. If optimal results are not achieved at any step, it may be recommended that the treatment is stopped/cancelled.

I. Ovulation Induction

The eggs are present in the ovaries within fluid-filled cysts called follicles. During a patient's menstrual cycle, usually one mature follicle develops, which results in the ovulation of a single egg. Several hormones including follicle stimulating hormone (FSH) and luteinizing hormone (LH) influence the growth of the ovarian follicle. These hormones are produced by the pituitary gland, which is located at the base of the brain. FSH is the main hormone that stimulates the growth of the follicle, which produces an estrogen hormone called *estradiol*. When the follicle is mature, a large amount of LH is released by the pituitary gland. This surge of LH helps to mature the egg and leads to ovulation 36-40 hours after its initiation.

There are two approaches for ovulation induction that are detailed below:

Medicated Approach - This is the most common approach to ovulation induction in a patient undergoing IUI. Medications are administered to increase the number of follicles that develop, which will increase the number of eggs that are released. There are several medications that can be used for this phase of treatment.

1. *Gonadotropins* - these are injectable medications commonly prescribed to stimulate the ovaries of women undergoing IVF treatment. Two types of gonadotropins can be prescribed and are discussed below.
 - a. FSH (Gonal-F[®], Follistim[®], Fertinex[®], Bravelle[®]) - These medications contain only FSH and are administered on a daily basis by injection.
 - b. LH (Luveris[®]) – This medication contains only LH and is administered by injection. It is used in combination with FSH containing medications.
 - c. Human Menopausal Gonadotropins (Pergonal[®], Repronex[®]) - These medications contain equal amounts of FSH and LH, and are administered on a daily basis by injection.
2. *GnRH Agonist (Lupron[®])* – This synthetic hormone is administered by an injection. The administration of Lupron initially causes release of FSH and LH from the pituitary gland. However, with continued administration there is a temporary depletion of FSH and LH, which suppresses a LH surge thereby preventing ovulation. Lupron is administered in conjunction with gonadotropins.

There are several ovulation induction protocols that utilize Lupron. The first involves the daily administration of Lupron beginning approximately one week before the anticipated menstrual period. Lupron is administered by itself until the menstrual period occurs generally 7-21 days later. After the

menstrual period occurs, the dose of Lupron is decreased and gonadotropins are started. When this protocol is used if there is a chance of sperm exposure vaginally it is advised that contraception be used following the menstrual period until the start of Lupron. For those patients with irregular menstrual cycles the Lupron can be started after a period is induced by progesterone or birth control pills. The second protocol involves a combination of a dilute dose of Lupron and gonadotropins started soon after the menstrual period has begun.

Although Lupron is approved by the Food and Drug Administration (FDA) for treatment of endometriosis, uterine fibroids, precocious puberty and prostate cancer in men, it is not FDA-approved for the treatment of infertility. However, most fertility centers in the United States and the world have used Lupron (or other GnRH agonists) for many years for this purpose.

3. *GnRH Antagonist (Cetrotide[®], Ganirelix[®])* - GnRH antagonists are medications that reversibly bind to GnRH receptors in the pituitary gland and prevent release of FSH and LH. GnRH antagonists are administered in combination with gonadotropins. The major benefit of a GnRH antagonist is that it suppresses a LH surge thereby preventing ovulation.
4. *Clomiphene Citrate (Clomid[®], Serophene[®])* and *letrozole (Famara[®])* - These medications are synthetic hormones that are taken orally for a period of five days and cause the release of FSH and LH, which stimulate the development of follicles. These medications are used in combination with injectable medications.
5. *Human Chorionic Gonadotropin [hCG] (Profasi[®], Ovidrel[®], Pregnyl[®], Novarel[®])* - This medication contains the pregnancy hormone, hCG, which functions similarly to LH. It is administered approximately 36 hours before the IUI by subcutaneous injection and matures the eggs, which will allow them to become fertilized.

Note: Many of the medications that are used are administered by an injection. The patient or another person can be instructed to give these injections.

Side Effects

The use of the above listed medications can cause side effects such as nausea, vomiting, hot flashes, headaches, mood swings, visual symptoms, memory difficulties, joint problems, weight gain and weight loss, all of which are temporary. Rare allergic reactions are also possible. Other possible side effects include the following:

Ovarian Hyperstimulation - After ovulation the follicles can fill up with fluid and form cysts. The formation of cysts will result in ovarian enlargement and can lead to lower abdominal discomfort, bloating and distention. These symptoms generally occur within two weeks after hCG administration. The symptoms usually resolve within 1-2 weeks without intervention. If ovarian hyperstimulation occurs your physician may recommend a period of reduced activity and bed rest. Pregnancy can worsen the symptoms of ovarian hyperstimulation. Severe ovarian hyperstimulation is characterized by the development of large ovarian cysts and fluid in the abdominal and, sometimes, chest cavities. Symptoms of severe ovarian hyperstimulation include abdominal distention and bloating along with weight gain, shortness of breath, nausea, vomiting and decreased urine output. Approximately 1-2% of patients will develop severe ovarian hyperstimulation and may need to be admitted to the hospital for observation and treatment. To help alleviate the symptoms of severe ovarian hyperstimulation an ultrasound-guided paracentesis can be performed which results in the removal of fluid from the abdominal cavity. Rare, but serious consequences of severe ovarian hyperstimulation include formation of blood clots that can lead to a stroke, kidney damage and possibly death. Every patient who takes these medications can develop ovarian hyperstimulation but the chance is higher in a patients with a high blood estradiol level and a large number of ovarian follicles. In some cases when the estradiol level is significantly elevated, the cycle may be cancelled or possibly converted to IVF.

Ovarian Torsion (Twisting) - In less than 1% of cases, a fluid filled cyst(s) in the ovary can cause the ovary to twist on itself. This can decrease the blood supply to the ovary and result in significant lower abdominal pain. Surgery may be required to untwist or possibly remove the ovary.

Ovarian Cancer- In the general population, every patient with ovaries has a 1 in 70 chance of developing ovarian cancer during their lifetime. Studies have shown that infertile patients with ovaries have a higher chance of developing ovarian cancer than fertile patients with ovaries. Controversial data exists that associates the use of ovulation induction drugs (e.g., clomiphene citrate, gonadotropins) with an increased risk of ovarian cancer. However, presently a cause and effect relationship has not been clearly established.

Non-Medicated Approach- Non-medicated IUI treatment is less commonly used than the medicated approach. If a patient has regular menstrual cycles, a non-medicated cycle may be considered. With this approach, the development of the single follicle is monitored with an ovulation predictor kit or blood tests and ultrasound examinations. When the follicle is mature and ovulation is imminent, the IUI treatment will be planned. In contrast to the medicated approach, there is a lower chance of pregnancy because only one egg is released for possible fertilization.

Monitoring- During the ovulation induction phase of treatment, monitoring of follicular development is performed with periodic blood hormone tests and/or vaginal ultrasound exams. Monitoring helps the physician to determine the appropriate dose of the medications and the timing of the egg retrieval. Vaginal ultrasound examinations are usually painless and generally considered to be safe. However, the possibility of harm cannot be excluded. Blood drawing may be associated with mild discomfort and, possibly, bruising, bleeding, infection or scar at the needle sites. The need for repeated ultrasound examinations and/or blood drawing on a frequent basis requires the patient's presence in the vicinity of a Boston IVF monitoring site.

II. INTRAUTERINE INSEMINATION

Around the time of ovulation, a patient receiving ovulation inducing medications will be instructed to either have intercourse if applicable or an intrauterine insemination (IUI) with a washed sperm sample. On the day of the IUI treatment, the partner who produces sperm will be asked to produce a semen specimen at home or at the Center. The semen sample can be produced at home as long as it can be brought into the center within 90 minutes of production. It is important that the semen sample is kept at body temperature during transport. The semen sample will then be washed and prepared. In some cases the patient (or couple if applicable) may elect to use a donor sperm sample.

To perform an IUI a speculum is placed into the vagina and the cervix is visualized. Sperm are loaded into a catheter, which is inserted through the cervical canal and into the uterine cavity. Following the insemination normal activity can be resumed. Because a catheter is inserted into the uterine cavity during the insemination treatment, there is always the risk of a pelvic infection following the treatment. Symptoms of an infection include fever, vaginal bleeding, chills and abdominal pain. If any of these symptoms occur you should contact your physician. If you should have any difficulty in contacting your physician you should proceed to the emergency department of the nearest hospital. In rare cases, hospitalization with intravenous antibiotics and/or surgery (to remove ovaries, fallopian tubes, or the uterus) may be necessary. As a result fertility may be impaired in some cases.

III. TREATMENT FOLLOWING OVULATION

Fourteen days after ovulation has occurred, a blood pregnancy test can be performed. If this test is found to be positive, a repeat pregnancy test may be done 2-3 days later. If the test results are rising appropriately, a vaginal ultrasound will be done approximately four weeks after the treatments to determine the status of the pregnancy. Because of the potential for complications following ovulation induction, the patient should have access to medical care up to the time of the pregnancy test and beyond if pregnancy is established. If travel is absolutely necessary, it should be discussed with a physician.

TREATMENT OUTCOMES

The success (the delivery of a live born infant) following a cycle of treatment with the administration of ovulation induction medications is between 5-20% per cycle. The development of a pregnancy following this treatment is dependent on many factors, some of which include: the age of the patient, the infertility diagnosis, the number of previous cycles of treatment, the number of follicles that develop, and the quality of the sperm used.

The following is a list of common events when pregnancy does not lead to the birth of a single baby:

Miscarriage - The risk of miscarriage in the general population is 15-20%. The risk of miscarriage increases with the age of the patient and for patients over 40 years of age, the risk may exceed 50%. Studies have shown either no increase or a slight increase in the risk of miscarriage in patients who conceive with this treatment. Most miscarriages are associated with lower abdominal cramping and bleeding, but do not necessarily require treatment. In some cases, however, complete removal of the pregnancy tissue must be accomplished by a surgical procedure called a dilatation and curettage (D&C) or dilatation and evacuation (D&E). This procedure is usually performed under anesthesia in the operating room and involves placing a suction tube into the uterine cavity to remove the pregnancy tissue.

Tubal (Ectopic) Pregnancy - An ectopic pregnancy may develop as a result of this treatment. The majority of ectopic pregnancies are present in the fallopian tube. The chance of tubal pregnancy is greater in a woman with damaged tubes. If a patient has a tubal pregnancy, they may need surgical treatment, which may involve the removal of the involved tube. Medical treatment with methotrexate may be an option in selected cases.

Multiple Pregnancy - The administration of ovulation induction medications can result in the ovulation of more than one egg, which increases the chance of a multiple pregnancy. The chance of multiple pregnancy ranges from 8-25%, which is in part dependent on the medication that is used. For instance, following clomiphene citrate treatment the multiple pregnancy rate ranges between 8-12%. When the injectable medications are used (gonadotropins) the multiple pregnancy rate is between 20-25%. Of the multiple pregnancies, approximately 80% are twins and the remainder (20%) are triplets and quadruplets. The chance of quadruplets is less than 2% of all pregnancies. Rarely, more than quadruplets can result. All multiple pregnancies are associated with an increased risk of most complications of pregnancy including but not limited to miscarriage, toxemia, congenital anomalies, gestational diabetes and premature labor and birth. Premature birth is the single greatest cause of death or disability in newborn infants. In contrast to a single intrauterine pregnancy, a multiple pregnancy may pose increased emotional and financial hardship.

If a multiple pregnancy develops, the patient (or couple if applicable) may consider being referred to a specialist who can perform a multi-fetal reduction procedure. This procedure, which is performed at approximately three months of pregnancy, is done to reduce the number of pregnancy sacs to a lower and safer number. Although this procedure is successful 90-95% of the time, a complete miscarriage may result. The best time to discuss the risks of multiple pregnancy and multifetal pregnancy reduction with your physician is before your treatment cycle begins.

Other Risks - Most infants who have been born following fertility treatment are normal. The rate of congenital abnormalities (birth defects) in the general population is 2-3% and is not different in babies conceived following this treatment. It is important to be aware that genetic abnormalities, structural abnormalities, mental retardation and other abnormalities may occur following this treatment or as they do in pregnancies conceived naturally.

Psychological Risks - Undergoing infertility treatment can be psychologically stressful. Anxiety and disappointment may occur at any point during and after treatment. Significant commitment of time and at times finances may be required. All patients (or couples if applicable) are encouraged to meet with a licensed counselor.

There are many complex and sometimes unknown factors, which may prevent the establishment of pregnancy. Known factors, which may prevent the establishment of pregnancy, include, but are not limited to, the following:

1. The ovaries may not respond to the medications or the ovarian follicles may not develop during the treatment.
2. The ovaries may over respond to the medication and the cycle may be cancelled because of the increased risk of ovarian hyperstimulation and/or multiple pregnancy.
3. If a partner producing sperm is applicable they may be unable to ejaculate or the semen sample from partner or sperm donor may be of poor quality.
4. The passage of the catheter into the uterus may be technically difficult or impossible.
5. Even if the insemination is successfully performed, pregnancy may not result.
6. If a pregnancy is established, it may not develop normally.
7. Equipment failure, infection, technical problems, human errors and/or other unforeseen factors may result in loss or damage to the semen sample.

The foregoing general information is based upon the experience and knowledge of the Boston IVF physicians. It is based, in part, upon a review of the literature pertaining to Reproductive Medicine. This information is generally accurate and comprehensive, however, medicine is a dynamic discipline and reproductive medicine in particular is constantly evolving. Estimates of risks factors and the relative benefits of alternative treatment that have been discussed with you represent the best professional judgment of the physicians and caregivers of Boston IVF taking into account your specific needs and circumstances.

ACKNOWLEDGEMENT OF INFORMED CONSENT AND AUTHORIZATION

I/We acknowledge that I/we, the undersigned, are voluntarily seeking treatment with **Ovulation Induction Medications and Intrauterine Inseminations** in order to conceive a child. I/We will acknowledge our natural parentage of any child or children born through this treatment.

I/We have discussed this treatment in detail with a Boston IVF physician and caregivers in language that we understand. I/We understand the purpose, risks and benefit of the treatment. **I/We acknowledge that we have read all pages of this consent form and all of our questions concerning the treatment have been fully answered to our satisfaction.**

I/We are aware that there are other centers in the area that offer this treatment and we have freely chosen to have the treatment at Boston IVF.

By consenting to treatment at Boston IVF I/we accept the responsibilities, conditions and risks involved as set out in this document and as explained by the staff of Boston IVF. In addition, I/we consent to the techniques and procedures used to accomplish this treatment described in this document and as explained by the physicians and staff of Boston IVF.

I/We understand and acknowledge that medicine is not an exact science and that in cases of doubt Boston IVF physicians and caregivers will exercise their best professional judgment.

I/We acknowledge and agree that acceptance into treatment and our continued participation is within the sole discretion of Boston IVF. I/We understand that should this cycle be unsuccessful, it may be determined that further treatment may not be indicated.

I/We agree to notify BIVF immediately in writing of any change in marital status including separation or divorce id applicable.

I/We also understand that I/we are financially responsible for any medical expenses that are not covered by our insurance policy.

In order to obtain required cycle outcome data we give Boston IVF consent to contact any physicians who provided care during and after a pregnancy.



Notarization Form (This form is only needed if not able to have witnessed at Boston IVF)

Patient Name (print) **Patient Signature** / /
Date of Birth (MM/DD/YYYY)

State of: _____ County of: _____

On this _____ day of _____ 20____, before me, the undersigned notary public, personally appeared _____, proved to me through satisfactory evidence of identification, which were _____, to be the person whose name is signed on the proceeding or attached document in my presence.

ID NUMBER: _____ Expiration Date: / /
(MM/DD/YYYY)

 / /
Today's Date (MM/DD/YYYY)

Notary Signature

Title
My appointment expires: / /
(MM/DD/YYYY)

Partner Name (if applicable, print) **Partner Signature** / /
Date of Birth (MM/DD/YYYY)

State of: _____ County of: _____

On this _____ day of _____ 20____, before me, the undersigned notary public, personally appeared _____, proved to me through satisfactory evidence of identification, which were _____, to be the person whose name is signed on the proceeding or attached document in my presence.

ID NUMBER: _____ Expiration Date: / /
(MM/DD/YYYY)

 / /
Today's Date (MM/DD/YYYY)

Notary Signature

Title
My appointment expires: / /
(MM/DD/YYYY)