Ovarian Superovulation Injectable Medications

General Information

Definitions:
Ovarian superovulation techniques are used to stimulate the ovaries to produce more than just a single egg. Menopur, Repronex, Follistim and Bravelle are examples of injectable hormones used in ovarian superovulation techniques. Menopur and Repronex contain both Luteinizing Hormone (LH) and Follicle Stimulation Hormone (FSH). Follistim, Bravelle and Gonal-F contain only FSH.

Indications:
The injectable medications are used in the induction of ovulation in women. Women with ovulatory difficulties or patients that desire to have more than one egg released in a given cycle may benefit from taking these medications. These medications may also be used with men whose fertility problems arise from pituitary or hypothalamic abnormalities.

Contraindications:
Women who have complete ovarian failure or are close to menopause and men who have testicular failure will not benefit from the administration of these medications. Individuals who have a history of hypersensitivity to any of these drugs should use the specific medication with caution.

Instructions:
We ask that you have a working answering machine for your home phone number and identify yourself clearly on the machine. Your medication dosage may need to be modified and an answering machine is the most consistent way for us to contact you.

**Cycle Day 1 (1st day of normal menstrual flow)**
Call to schedule a baseline vaginal ultrasound for Cycle Day 2 or 3. If cycle day 1 falls on a Friday, please call us ASAP so that we may perform a baseline ultrasound and teaching on that same day, rather than over the weekend. If your flow starts on Saturday, you can call after 8:30 a.m. on Monday, unless you were specifically told that you needed to baseline by day 2 or Monday is a holiday and the practice is closed to routine patients. If you start on Sunday, please wait until Monday to call. We will always see you, 365 days of each year.

**Cycle Day 1, 2 or 3 (note: A vaginal ultrasound requires an empty bladder.)**
If the ultrasound scan does not show any enlarged ovarian cysts, you will be provided instructions and prescriptions (if not already provided) for all of your medications, needles and syringes. The majority of patients have the medications administered by their spouses or
friends. Please bring your medications and have the person who is to help you administer the medications present for teaching during this baseline ultrasound appointment.

The best time for administration of the medication is during the evening around 6-8:00 p.m. This will allow for us to contact you regarding any modification of your dosage. The general dilution for Repronex is 75 International Units (IU's) mixed per 0.5 cc of solution with these medications injected into the muscle (intramuscular: IM). Menopur, Follistim, Bravelle, and Gonal-F may be either injected into the superficial fat (subcutaneous: SC) or IM:

<table>
<thead>
<tr>
<th>Repronex (use a 3 cc syringe)</th>
<th>Menopur, Bravelle, Follistim &amp; Gonal-F (use a 3 cc syringe)</th>
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<tbody>
<tr>
<td>75 IU in 1.0 cc</td>
<td>75 IU in 1.0 cc</td>
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<tr>
<td>150 IU in 1.0 cc</td>
<td>150 IU in 1.0 cc</td>
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<tr>
<td>225 IU in 1.5 cc’s</td>
<td>225 IU in 1.0 cc</td>
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<tr>
<td>300 IU in 2.0 cc’s</td>
<td>300 IU in 1.0 cc</td>
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Repronex is the only medication that needs to be injected into the muscle while the rest can be injected into the subcutaneous fat. Your physician will choose which route of administration is best based on your particular history and physical characteristics. The IM medications are normally injected deep into the muscle of the buttocks and occasionally in the muscle of the thigh. Injections over 300 units are generally split between two injections. The SC medications can be administered into the fat on the back of the arm and the abdominal regions.

**Upcoming Cycle Days**

Between the fourth and the sixth day of injections, you will need to be seen in the office between 8:00-9:00 a.m. for an ultrasound and possible estrogen blood test. As best as we are able to accommodate, your referring physician may perform ultrasounds and bloods may be drawn out-of-town and sent to our lab or the appropriate laboratory for testing. Blood test results, instructions regarding the modifications of the medication dosages, the scheduling of future ultrasounds and blood tests will be called to you between 4:00 & 4:45 p.m. that same day. Please do not call us prior to 4:45 p.m. for your test results. The ultrasounds and estrogen blood draws will generally continue every two or three days until you are close to ovulation.

The average number of days of injections is about 8-10 although wide ranges are common.

Once the ovaries are sufficiently stimulated, you will be given human Chorionic Gonadotropin (hCG) in order to trigger your ovulation. If your ovaries have become overly stimulated and you are at risk for the ovarian hyperstimulation syndrome (see below), hCG will not be given and the cycle will be canceled. This happens in about 1% of the patients.

Therapy such as intra-uterine insemination (IUI) will be scheduled about 36 hours after the HCG injection. You will not need to take any ovarian superovulation medications on the evening or in the days following the hCG injection.

**Complications:**
When a pregnancy does occur, the chance of having a multiple gestation is approximately 20%. About 75-90% of these are twins with the remainder triplets and rarely more. A multiple gestation places the mother at a higher risk of hypertension, premature labor, toxemia, a surgical delivery and other pregnancy complications. For the babies, there is an increased risk of prematurity and all the complications that occur with the delivery of a premature infant. If a multifetal pregnancy occurs (three or more), fetal reduction may need to be considered. Please understand that fetal reduction is discussed in fewer than 4% of all pregnancies achieved through this facility.

These hormones are potent agents capable of causing mild to severe adverse reactions in women. Careful monitoring of the ovarian response using estrogen levels and ultrasounds will minimize the risks, but not eradicate them. Ovarian over stimulation essentially occurs in almost all the women to some degree. A true Ovarian HyperStimulation Syndrome (OHSS) is uncommon (1%) and usually presents with abdominal distention, pain and weight gain. Under severe circumstances, hospitalization may occur. When this occurs, the ovaries become quite large and fluid leaks into the abdominal and other body cavities. In the most severe of cases, electrolytes may become out of balance, fluid may also collect around the lungs and heart, the ovarian cysts may rupture requiring surgery, blood vessels may clot off leading to loss of a limb, stroke, and rarely death. These extreme consequences rarely occur. The symptoms of OHSS may be more prolonged and severe if pregnancy occurs during the stimulation cycle.

Breast tenderness and shorter or longer cycles are frequent findings for those of our patients who undergo superovulation. A rash may develop at the sight of the injection indicating an irritation or perhaps an allergy to the medication. This is exceedingly rare and should be communicated to our office if consistently seen.

There is no evidence that taking these medications pose a direct risk to the fetus. There is no increased incidence of genetically abnormal infants or congenital abnormalities in infants conceived with these medications.

There is no evidence of an increased risk for breast or uterine cancers or premature menopause when these medications are used. The theoretical risks of ovarian cancer are covered on a separate information sheet and remain only conjecture. If desired, please ask the nurses for a copy of this information sheet. In general, the risks, if they exist at all, are minimal.

**Summary:**
The decision to use these medications is often difficult. The costs and the risks noted above must be balanced with the expected benefits.