

PATIENT INFORMATION ♦ FSH/HMG CYCLES

Definitions:

1. FSH/HMG can be Repronex, Menopur, Bravelle, Gonal-F, Follistim vials and Pen, and other brand names.
2. HCG can be Ovidrel and other brand names.

Protocol for Patients Starting FSH/HMG:

1. Your account must be *paid in full* before starting a FSH/HMG cycle.
2. If you have questions as to why you need this treatment, consult with your physician. This treatment is an injectable fertility drug needing frequent monitoring.
3. After your appointment, the nurse needs to make an appointment with you and your partner for a FSH/HMG class (even if you do not plan to start soon). Please read the remainder of the information provided here before your FSH/HMG instruction class.
4. You and your partner need to have the class well before the day you are ready to start the medication.

Purpose of Fertility Medications:

Clomiphene citrate (Clomid or Serophene) and human menopausal gonadotropins (FSH/HMG) are prescribed to stimulate the development and release of an egg(s) from the ovary. Clomiphene is a synthetic product that stimulates the hypothalamus in the brain to trigger the release of FSH (follicle stimulating hormone) and LH (luteinizing hormone) from the pituitary gland. These two hormones stimulate the ovary, causing follicles to develop in the ovary. FSH is manufactured using DNA technology. HMG is extracted from the urine of menopausal women and then freeze-dried in sterile glass ampules where it is sealed until use. The action of HCG is similar to that of pituitary LH, which is the hormone that triggers ovulation or the actual release of the egg(s) from the ovary. FSH/HMG is a fertility medication containing FSH that may be prescribed by your physician.

FSH/HMG Cycles:

A prescribed dosage of FSH/HMG is taken for 3-5 days initially, after which an ultrasound and estrogen level are obtained. This is usually followed by additional daily doses of FSH/HMG until follicles are mature and estrogen levels are adequate, at which point HCG is administered to trigger ovulation. Again, FSH/HMG is usually begun on cycle day 3, 4 or 5.

Pre-cycle Screening:

You will be required to have a screening ultrasound before starting your medication to make sure you have no ovarian cysts. You also may be required to have an FSH and/or estrogen level before starting your medication. If these test results are elevated, you will be asked to wait out a cycle and call again at the start of your next menses.

Required Monitoring:

The key to successful induction of ovulation with FSH/HMG is to adjust the ovarian stimulation to an ideal level and then to administer the ovulating dose of HCG. Too low a level of stimulation leads to poor follicle growth and poor pregnancy outcome, while too high a level of stimulation can lead to a multiple gestation or hyperstimulation syndrome. At our clinic, blood estradiol levels and ovarian ultrasounds (follicular scans) are done to evaluate response to FSH/HMG and the level of stimulation. Eggs develop inside fluid filled sacs called follicles on the ovary. Ultrasound exams allow measurement of these follicles. Your physician would ideally like to see estrogen levels between 150 and

250 pg/ml per mature follicle and ovarian follicles measuring an average of at least 15 mm at the time of your HCG injection. The availability of this type of monitoring requires highly skilled staff and expensive equipment, which has limited the number of centers that can use FSH/HMG for induction of ovulation.

In order to get results of your estrogen level the same day that your blood is drawn, you must have your blood drawn by 10 a.m. at RiverPlace. You will get an appointment for your ultrasound usually between 7:30-9:45 a.m. at RiverPlace. The ultrasound has the ability to measure follicles utilizing a vaginal probe. This monitoring is vitally important to prevent complications of FSH/HMG therapy. Monitoring can sometimes be arranged elsewhere if you live a long distance away. This can only be done if we can get the estradiol results and ultrasound before 2 p.m. the same day.

Major Side-effects Associated with FSH/HMG:

The major risks of FSH/HMG therapy relate to the stimulation of the ovary. A certain degree of stimulation is required to produce the desired number of follicles, but over-stimulation can lead to two major risks:

1. **MULTIPLE GESTATION** - The multiple gestation rate is approximately 10-25% with FSH/HMG. The majority of these will be twins, however multiple gestations greater than twins are possible.
2. **OVARIAN HYPERSTIMULATION SYNDROME (OHSS)** - OHSS is characterized by ovarian enlargement and fluid in the abdomen, with or without pain. This fluid is lost from the bloodstream that can cause the blood to become overly thick and concentrated. Symptoms of this syndrome occur 2-5 days after the HCG injection and are usually mild and subside spontaneously within 1 or 2 weeks. Severe OHSS requires hospitalization for bed rest and fluid monitoring. Careful monitoring with estrogen levels and ultrasounds can detect problems early, thus avoiding serious problems in most cases. After your HCG injection, you *may* be asked to weigh yourself and measure your abdominal girth daily. Notify your physician immediately if your weight has increased by 5-lbs. or more within 1 or 2 days, or if you are experiencing significant bloating or discomfort, and shortness of breath.

Preparing FSH/HMG for Injection:

The FSH/HMG comes as a dry powder in a sealed glass ampule. The medication can be purchased in ampules of 75 IU each. Each package also contains an ampule containing 1 cc of diluent. The ampules are marked with a blue dot, indicating where they should break. Point the blue dot away from you and break the top off the ampule by pulling the top toward you (the broken edge should point away from you). Be careful not to cut yourself on the sharp glass edges. Use 1 cc of diluent to mix up to 4 ampules FSH to be injected. If you are using HMG, use ½ cc of diluent for each ampule of powder. Prepare a syringe as demonstrated at your FSH/HMG consult. Withdraw the appropriate amount of diluent and add to the ampule(s) of FSH/HMG. The medication dissolves very quickly. Draw the solution back into your syringe, and change needles as demonstrated at your consult. Clear the syringe of all air and replace the cover over the needle. You are now ready to give the injection. If you are using more than 1 ampule of FSH/HMG, draw up the appropriate amount of diluent and inject into the first ampule of medication. Draw it all back out and inject it into the second ampule of medication. Draw it all back out, clear the syringe of air and change the needle. You are now ready to give the injection.

Preparation and Administration of HCG:

Ovidrel 250 mcg comes in a premixed syringe and is given by subcutaneous injection (short needle). This is only taken when the doctor recommends it.

Subcutaneous Injection Technique:

Gonal-F is given by subcutaneous injection. This means it is injected with a small needle between the fat and muscle layer, usually in the abdomen or upper arm. The needles are so short they can be put straight in and then push in the plunger.

Using a Follistim AQ Pen with multiple dose cartridges is an option most patients like. The pen and needles are free and there are 300 IU and 600 IU cartridges. The Medical Assistant or Nurse working with you can help with the number of cartridges that you may need for a cycle. The dosage is dialed in on the pen and you then do a subcutaneous (short needle) injection. If there is not enough medication in the current cartridge that you are using for the full dosage, the dial on the pen will not return to zero. You then insert a new cartridge and without changing the dial, inject the remainder of your medication. If you are getting your medications from a pharmacy, be sure to buy enough cartridges to finish your cycle. We will call your medication in with refills. This medication delivery system is so good that most patients respond with less medication versus using ampules or vials.

Possible Association with Ovarian Tumors:

A review of three studies performed in 1987-89 has suggested that women who have used fertility drugs have an increased risk of ovarian cancer¹. However, this conclusion is very uncertain because the number of cases is very small. Furthermore, the exact drugs and dosage used by these cases are unknown. Because pregnancy and the use of oral contraceptives both prevent ovulation and provide protection against ovarian cancer, it is reasonable to be concerned that multiple ovulations might carry some risk. At best, the data raise this as a possibility, but by no means, is it certain that there is an increased risk. It is important to be aware that in 2,632 women in Israel treated for infertility, no association was subsequently found between any cancer and ovulation-inducing drugs². Finally, to this date, there have been no cases of ovarian cancer reported in women who have previously undergone treatment with fertility drugs for In vitro fertilization and related procedures.

¹ Whittemore AS, Harris P, Itnyre J, and the Collaborative Ovarian Cancer Group, Collaborative analysis of twelve U.S. case-control studies. II. Invasive epithelial ovarian cancers in white women. *Am J Epidemiol* 1992;136:1184.

² Ron E, Lunenfeld B, Menczer J, et al.: Cancer incidence in a cohort of infertile women. *Am J Epidemiol* 1987;125:780.

There is no way to know how you will respond to FSH/HMG. Your physician will be making the decisions about how much medication you will be instructed to take and also about stopping the medication if your response is poor, or if you over-respond and are at too great a risk for multiple birth or hyperstimulation to continue the FSH/HMG cycle. Not all cycles are ideal. Roughly 20-30% of cycles are not adequate due to failure of estrogen levels to rise, or when estrogen levels rise but then drop suddenly, or if follicles fail to grow. Adjustments in subsequent cycles may be necessary to improve the outcome.

Call the nurse the day your period begins, or on Monday if your period begins on a weekend. Depending on your response in the last FSH/HMG cycle, your physician will adjust your dosage. A screening ultrasound will be needed before beginning FSH/HMG again to be sure there are no residual cysts remaining. If residual cysts are discovered, your physician may require that you wait out a cycle before attempting another cycle. If your temperature rise is sustained for more than two weeks and your period has not begun, pregnancy must be suspected. Do a home pregnancy test and if positive, you should call the clinic nurse to arrange a blood pregnancy test.

Be sure you always have enough medication on hand during your cycle.

Good luck with your efforts at achieving pregnancy, and feel free to call the clinic if further questions or concerns arise at (503) 418-3700. For evening/weekend emergencies, call the paging operator at (503) 494-8311.

If you get your medication from a pharmacy, you can purchase from the clinic all the syringes, needles and alcohol sponges you will need for a complete cycle for \$20. You can pick them up when you come for your baseline scan.

Average number of days patients take FSH is 8 to 10.	AVERAGE FSH/HMG CYCLE		
	50 IU per day	125 IU per day	175 IU per day
MEDICATIONS (10 Days): <ul style="list-style-type: none"> FSH (Follistim) HMG (Repronex) Ovidrel (HCG) 	10 days @ 600 IU = \$544 10 days @ \$42 per 75 IU = \$420 1 @ \$75	10 days @ 1200 IU = \$1,088 10 days @ \$42 per 75 IU = 840 1 @ \$75	10 days @ 1750 IU = \$1,632 10 days @ \$42 per 75 IU = \$1,260 1 @ \$75
MONITORING: <ul style="list-style-type: none"> Estradiol Ultrasound Scan Venipuncture 	3 @ \$70/unit = \$210 4 @ \$250/unit = \$1,000 3 @ \$15/each = \$45	3 @ \$70/unit = \$210 4 @ \$250/unit = \$1,000 3 @ \$15/each = \$45	3 @ \$70/unit = \$210 4 @ \$250/unit = \$1,000 3 @ \$15/each = \$45
PLEASE NOTE that the University Fertility Consultants (the physicians) use the University Andrology Lab for most lab work requested by the physician. The University Fertility Consultants participates with several insurance companies. The University Andrology Lab is not a participating provider . As a courtesy, the Lab will bill your insurance for reimbursement. You may want to contact your insurance to see how this non-participating status may affect your reimbursement level.			
FSH/HMG Management (each cycle)	\$300	\$300	\$300

(FSH) Follistim Cartridge:

- 600 IU = \$544*
- 300 IU = \$272*

* Equals \$68 per 75 IU.

(HMG) Repronex:

- 75 IU = \$42

INSTRUCTION CLASS (one time fee) \$25 to \$50 based on amount of time needed.