

	Ganirelix Acetate 250 mcg
Serum LH (mIU/mL) on day of hCG [‡]	1.6
5 th –95 th percentiles	0.6–6.9
No. of subjects with LH rise \geq 10 mIU/mL [†]	13
No. of follicles $>$ 11 mm [§]	10.7 (5.3)
No. of subjects with oocyte retrieval	440
No. of oocytes [¶]	8.7 (5.6)
Fertilization rate	62.1%
No. subjects with ET [¶]	399
No. of embryos transferred [¶]	2.2 (0.6)
No. of embryos [¶]	6.0 (4.5)
Ongoing pregnancy rate ^{¶§}	
per attempt, n (%) [¶]	94 (20.3)
per transfer, n (%)	93 (23.3)
Implantation rate (%) [¶]	15.7 (29)

(Protocol 38607)

* Following initiation of Ganirelix Acetate therapy

† Median values

§ Restricted to subjects with hCG injection

¶ Mean (standard deviation)

† ET: Embryo Transfer

¶ As evidenced by ultrasound at 12–16 weeks following ET

λ Includes one patient who achieved pregnancy with intrauterine induction

Some centers were limited to the transfer of \leq 2 embryos based on local practice standards

The mean number of days of Ganirelix Acetate treatment was 5.4 (2–14).

LH Surges

The midcycle LH surge initiates several physiologic actions including: ovulation, resumption of meiosis in the oocyte, and luteinization. In 463 subjects administered Ganirelix Acetate Injection 250 mcg, a premature LH surge prior to hCG administration, (LH rise \geq 10 mIU/mL with a significant rise in serum progesterone $>$ 2 ng/mL, or a significant decline in serum estradiol) occurred in less than 1% of subjects.

INDICATIONS AND USAGE

Ganirelix Acetate Injection is indicated for the inhibition of premature LH surges in women undergoing controlled ovarian hyperstimulation.

CONTRAINDICATIONS

Ganirelix Acetate Injection is contraindicated under the following conditions:

- Known hypersensitivity to Ganirelix Acetate or to any of its components.
- Known hypersensitivity to GnRH or any other GnRH analog.
- Known or suspected pregnancy (see PRECAUTIONS).

WARNINGS

Ganirelix Acetate Injection should be prescribed by physicians who are experienced in infertility treatment. Before starting treatment with Ganirelix Acetate, pregnancy must be excluded. Safe use of Ganirelix Acetate during pregnancy has not been established (see CONTRAINDICATIONS and PRECAUTIONS).

PRECAUTIONS

General

Special care should be taken in women with signs and symptoms of active allergic conditions. Cases of hypersensitivity reactions (both generalized and local), including anaphylaxis (including anaphylactic shock), angioedema and urticaria, have been reported with Ganirelix Acetate, as early as with the first dose, during post-marketing surveillance (see ADVERSE REACTIONS). If a hypersensitivity reaction is suspected, Ganirelix Acetate should be discontinued and appropriate treatment administered. In the absence of clinical experience, Ganirelix Acetate treatment is not advised in women with severe allergic conditions.

Packaging components of this product are free from dry natural rubber/latex.

Information for Patients

Prior to therapy with Ganirelix Acetate Injection, patients should be informed of the duration of treatment and monitoring procedures that will be required. The risk of possible adverse reactions should be discussed (see ADVERSE REACTIONS).

Ganirelix Acetate should not be prescribed if the patient is pregnant.

Laboratory Tests

A neutrophil count \geq 8.3 ($\times 10^9/L$) was noted in 11.9% (up to $16.8 \times 10^9/L$) of all subjects treated within the adequate and well-controlled clinical trials. In addition, downward shifts within the Ganirelix Acetate Injection group were observed for hematocrit and total bilirubin. The clinical significance of these findings was not determined.

Drug Interactions

No formal drug-drug interaction studies have been performed.

Carcinogenesis and Mutagenesis, Impairment of Fertility

Long-term toxicity studies in animals have not been performed with Ganirelix Acetate Injection to evaluate the carcinogenic potential of the drug. Ganirelix Acetate did not induce a mutagenic response in the Ames test (*S. typhimurium* and *E. coli*) or produce chromosomal aberrations in *in vitro* assay using Chinese Hamster Ovary cells.

Pregnancy

Ganirelix Acetate Injection is contraindicated in pregnant women. When administered from Day 7 to near term to pregnant rats and rabbits at doses up to 10 and 30 mcg/day (approximately 0.4 to 3.2 times the human dose based on body surface area), Ganirelix Acetate increased the incidence of litter resorption. There was no increase in fetal abnormalities. No treatment-related changes in fertility, physical, or behavioral characteristics were observed in the offspring of female rats treated with Ganirelix Acetate during pregnancy and lactation.

The effects on fetal resorption are logical consequences of the alteration in hormonal levels brought about by the antagonadotropic properties of this drug and could result in fetal loss in humans. Therefore, this drug should not be used in pregnant women (see CONTRAINDICATIONS).

Nursing Mothers

Ganirelix Acetate Injection should not be used by lactating women. It is not known whether this drug is excreted in human milk.

Geriatric Use

Clinical studies with Ganirelix Acetate Injection did not include a sufficient number of subjects aged 65 and over.

ADVERSE REACTIONS

The safety of Ganirelix Acetate Injection was evaluated in two randomized, parallel-group, multicenter controlled clinical studies. Treatment duration for Ganirelix Acetate ranged from 1 to 14 days. Table IV represents adverse events (AEs) from first day of Ganirelix Acetate administration until confirmation of pregnancy by ultrasound at an incidence of \geq 1% in Ganirelix Acetate-treated subjects, as early as with the first dose (see PRECAUTIONS).

TABLE IV: Incidence of common adverse events (incidence \geq 1% in Ganirelix Acetate-treated subjects). Completed controlled clinical studies (All-subjects-treated group).

Adverse Events Occurring in \geq 1%	Ganirelix Acetate N=794 % (n)
Abdominal Pain (gynecological)	4.8 (38)
Death Fetal	3.7 (29)
Headache	3.0 (24)
Ovarian Hyperstimulation Syndrome	2.4 (19)
Vaginal Bleeding	1.8 (14)
Injection Site Reaction	1.1 (9)
Nausea	1.1 (9)
Abdominal Pain (gastrointestinal)	1.0 (8)

During post-marketing surveillance, rare cases of hypersensitivity reactions, including anaphylaxis (including anaphylactic shock), angioedema and urticaria have been reported with Ganirelix Acetate, as early as with the first dose (see PRECAUTIONS).

Congenital Anomalies

An observational study in more than 1000 newborns compared the incidence of congenital anomalies in newborns of women administered Ganirelix Acetate to historical controls of a GnRH agonist. This study demonstrated that the incidence of congenital anomalies in children born after COH treatment in women using Ganirelix Acetate was comparable with that reported after a COH treatment cycle using a GnRH agonist.

The incidence of congenital malformations after some Assisted Reproductive Technologies (ART) (specifically *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI)) may be slightly higher than after spontaneous conception. This slightly higher incidence is thought to be related to differences in parental characteristics (e.g., maternal age, maternal and paternal genetic background, sperm characteristics) and to the higher incidence of multi-fetal gestations after IVF or ICSI. The causal relationship between these congenital anomalies and Ganirelix Acetate injection is unknown.

To report SUSPECTED ADVERSE EVENTS, contact Mullan Pharmaceutical Inc. at +1-800-673-9839 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

There have been no reports of overdosage with Ganirelix Acetate injection in humans.

DOSAGE AND ADMINISTRATION

After initiating FSH therapy on Day 2 or 3 of the cycle, Ganirelix Acetate injection 250 mcg may be administered subcutaneously once daily during the mid to late portion of the follicular phase. By taking advantage of endogenous pituitary FSH secretion, the requirement for exogenously administered FSH may be reduced. Treatment with Ganirelix Acetate should be continued daily until the day of hCG administration. When a sufficient number of follicles of adequate size are present, as assessed by ultrasound, final maturation of follicles is induced by administering hCG. The administration of hCG should be withheld in cases where the ovaries are abnormally enlarged on the last day of FSH therapy to reduce the chance of developing OHSS (Ovarian Hyperstimulation Syndrome).

Directions for Using Ganirelix Acetate Injection

1. Ganirelix Acetate injection is supplied in a single dose, sterile, prefilled syringe and is intended for SUBCUTANEOUS administration only.
2. Air bubble(s) may be seen in the pre-filled syringe. This is expected, and removal of the air bubble(s) is not needed.
3. Wash hands thoroughly with soap and water.
4. The most convenient sites for SUBCUTANEOUS injection are in the abdomen around the navel or upper thigh.
5. The injection site should be swabbed with a disinfectant to remove any surface bacteria. Clean about two inches around the point where the needle will be inserted and let the disinfectant dry for at least one minute before proceeding.
6. With syringe held upward, remove needle cover.
7. Pinch up a large area of skin between the finger and thumb. Vary the injection site a little with each injection.
8. The needle should be inserted at the base of the pinched-up skin at an angle of 45–90° to the skin surface.
9. When the needle is correctly positioned, it will be difficult to draw back on the plunger. If any blood is drawn into the syringe, the needle tip has penetrated a vein or artery. If this happens, withdraw the needle slightly and reposition the needle without removing it from the skin. Alternatively, remove the needle and use a new, sterile, prefilled syringe. Cover the injection site with a swab containing disinfectant and apply pressure; the site should stop bleeding within one or two minutes.
10. Once the needle is correctly placed, depress the plunger slowly and steadily, so the solution is correctly injected and the skin is not damaged.
11. Pull the syringe out quickly and apply pressure to the site with a swab containing disinfectant.
12. Use the sterile, prefilled syringe only once. Discard the unused portion and dispose of it properly.

HOW SUPPLIED

Ganirelix Acetate injection is supplied in:

Disposable, ready for use, single dose, sterile, prefilled 1 mL glass syringes containing 250 mcg/0.5 mL aqueous solution of Ganirelix Acetate closed with a rubber piston that does not contain latex. Each Ganirelix Acetate sterile, prefilled syringe is affixed with a 27 gauge x 1/2-inch needle closed by a needle shield.

Packaging components of this product are free from dry natural rubber/latex.

Single Syringe NDC 83301-0082-1

Storage

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Protect from light.

Manufactured for:

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Manufactured by:

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