NEW ZEALAND DATA SHEET

1 NAME OF THE MEDICINE

Ganirelix-AFT 250 µg/0.5 mL solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ganirelix (as the acetate salt) 0.5 mg/mL.

Ganirelix-AFT contains the synthetic decapeptide ganirelix (INN) as its acetate salt, with high antagonistic activity to the naturally occurring gonadotropin releasing hormone (GnRH).

Each prefilled syringe contains 250 µg ganirelix (as acetate) in 0.5 mL.

The amino acids at positions 1, 2, 3, 6, 8 and 10 of the natural GnRH decapeptide have been substituted resulting in N-Ac-D-Nal(2)[1], D-pClPhe[2], D-Pal(3)[3], D-hArg(Et2)[6], L-hArg(Et2)[8], D-Ala[10]]-GnRH with a molecular weight of 1570.4.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Solution for injection.

Ganirelix-AFT (ganirelix acetate) is presented as a sterile, ready for use, clear and colourless aqueous solution intended for subcutaneous administration.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

The prevention of premature luteinizing hormone (LH) surges in women undergoing controlled ovarian hyperstimulation (COH) for assisted reproduction techniques (ART).

In clinical trials, ganirelix was used with recombinant follicle stimulating hormone (FSH).

4.2 DOSE AND METHOD OF ADMINISTRATION

Ganirelix-AFT should only be prescribed by a specialist experienced in the treatment of infertility.

Dosage

Ganirelix-AFT is used to prevent premature LH surges in patients undergoing COH. Controlled ovarian hyperstimulation with FSH may start at day 2 or 3 of menses. Ganirelix-AFT (0.25 mg) should be injected subcutaneously once daily, starting on day 6 of FSH administration. In high responders an early LH rise may be prevented by starting Ganirelix-AFT treatment on day 5.

The start of Ganirelix-AFT may be delayed in the absence of follicular growth. Ganirelix-AFT and FSH should be administered at approximately the same time. However, the preparations should not be mixed and different injection sites are to be used. FSH dose

adjustments should be based on the number and size of growing follicles, rather than on the amount of circulating estradiol (see 5.1 Pharmacodynamic properties).

Daily treatment with Ganirelix-AFT should be continued up to the day that sufficient follicles of adequate size are present. Final maturation of follicles can be induced by administering human chorionic gonadotrophin (hCG). Because of the half-life of ganirelix, the time between two Ganirelix-AFT injections as well as the time between the last Ganirelix-AFT injection and the hCG injection should not exceed 30 hours, as otherwise a premature LH surge may occur. Therefore, when injecting Ganirelix-AFT in the morning, treatment with Ganirelix-AFT should be continued throughout the gonadotrophin treatment period including the day of triggering ovulation. When injecting Ganirelix-AFT in the afternoon, the last Ganirelix-AFT injection should be given in the afternoon prior to the day of triggering ovulation.

Ganirelix-AFT has been shown to be safe and effective in patients undergoing multiple treatment cycles. Luteal phase support should be given according to the reproductive medical centre's practice.

Special populations

Use in hepatic impairment

See 4.3 Contraindications.

Use in renal impairment

See 4.3 Contraindications.

Use in the elderly

No data available.

Paediatric population

There is no relevant use of Ganirelix-AFT in the paediatric population.

Effects on laboratory tests

No data available

Method of administration

Inspect the solution before use. It must only be used if it is clear and without particulate matter.

Ganirelix-AFT should be administered subcutaneously, preferably in the upper leg. The injection site should be varied to prevent lipoatrophy. The patient or her partner may perform the injections of Ganirelix-AFT themselves, provided that they are adequately instructed and have access to expert advice.

4.3 CONTRAINDICATIONS

- Hypersensitivity to the active substance or to any of the components including elastomer or rubber (see Section 6.1 List of Excipients and Section 6.5 Nature and Contents of Container).
- Hypersensitivity to GnRH or any other GnRH analogue

- Pregnancy or lactation
- Moderate to severe renal impairment and hepatic impairment

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Special care should be taken in women with signs and symptoms of active allergic conditions. Cases of hypersensitivity reactions (both generalised and local) have been reported with ganirelix injection, as early as with the first dose, during post-marketing surveillance. These events have included anaphylaxis (including anaphylactic shock), angioedema, and urticaria (See Section 4.8 Adverse Effects (Undesirable Effects)). If a hypersensitivity reaction is suspected, Ganirelix-AFT should be discontinued and appropriate treatment administered. In the absence of clinical experience, Ganirelix-AFT treatment is not advised in women with severe allergic conditions.

The needle shield of Ganirelix-AFT contains elastomer and rubber piston contains bromobutyl rubber which come into contact with this product and may cause allergic reactions (see Section 4.3 Contraindications and Section 6.5 Nature and Contents of Container).

Ovarian hyperstimulation syndrome (OHSS) may occur during or following ovarian stimulation. OHSS must be considered an intrinsic risk of gonadotrophin stimulation. OHSS should be treated symptomatically, e.g. with rest, intravenous infusion of electrolyte solutions or colloids and heparin.

Since infertile women undergoing assisted reproduction, and particularly IVF, often have tubal abnormalities the incidence of ectopic pregnancies might be increased. Early ultrasound confirmation that a pregnancy is intrauterine is therefore important.

The incidence of congenital malformations after Assisted Reproductive Technologies (ART) may be slightly higher than after spontaneous conceptions. This slightly higher incidence is thought to be related to differences in parental characteristics (e.g. maternal age, sperm characteristics) and to the higher incidence of multiple gestations after ART. There are no indications that the use of GnRH antagonists during ART is associated with an increased risk of congenital malformations. In clinical trials investigating more than 1000 newborns it has been demonstrated that the incidence of congenital malformations in children born after COH treatment using Ganirelix-AFT is comparable with that reported after COH treatment using a GnRH agonist.

The safety and efficacy of Ganirelix-AFT have not been established in women weighing less than 50 kg or more than 90 kg (see also 5.1 Pharmacodynamic properties and 5.1 Pharmacokinetic properties).

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Interactions of Ganirelix-AFT with other medicines have not been investigated; interactions with commonly used medicinal products, cannot therefore be excluded.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Ganirelix treatment of female rats resulted in reversible impairment of mating and fertility at a subcutaneous dose of 2.5 µg/kg/day, and reversible cessation of mating was seen in males treated with a subcutaneous dose of 0.1 mg/kg/day.

Use in pregnancy

Category D

Ganirelix-AFT is not intended to be used during pregnancy (see 4.3 Contraindications). No clinical data on exposed pregnancies are available.

In animals, exposure to ganirelix at the time of implantation resulted in litter resorption (see 5.3 Preclinical Safety Data). The relevance of these data for humans is unknown.

Use in lactation

Ganirelix-AFT should not be used by lactating women (see 4.3 Contraindications). It is not known whether ganirelix is excreted in breast milk.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of Ganirelix-AFT on ability to drive and use machines have not been studied.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

General disorders and administration site conditions

Ganirelix-AFT may cause a local skin reaction at the site of injection (predominantly redness, with or without swelling). In clinical studies, one hour after injection, the incidence of at least once of a moderate or severe local skin reaction per treatment cycle was 12% in ganirelix treated patients and 25% in patients treated subcutaneously with a GnRH agonist. The local reactions generally disappear within 4 hours after administration. Malaise was reported in 0.3% of patients.

Immune system disorders

Very rarely, post-marketing cases of hypersensitivity reactions (including rash, facial swelling, dyspnea, anaphylaxis (including anaphylactic shock), angioedema, and urticaria) have been reported, as early as with the first dose, among patients administered ganirelix.

Nervous system disorders

Headache (0.4%).

Gastrointestinal disorders

Nausea (0.5%).

Other reported undesirable effects are related to the controlled ovarian hyperstimulation

treatment for ART, notably pelvic pain, abdominal distension, OHSS, ectopic pregnancy and spontaneous abortion (see also section 4.4 Special warnings and precautions for use).

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at https://pophealth.my.site.com/carmreportnz/s/.

4.9 OVERDOSE

Overdose in humans may result in a prolonged duration of action. In case of overdose, Ganirelix-AFT treatment should be (temporarily) discontinued.

No data on acute toxicity of Ganirelix-AFT in humans are available but it is unlikely that toxic effects will occur. Clinical studies with subcutaneous administration of ganirelix at single doses up to 12 mg did not show undesirable systemic side-effects. In acute toxicity studies in rats and monkeys, non-specific toxic symptoms were only observed after intravenous administration of ganirelix over 1 and 3 mg/kg, respectively.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: anti-gonadotrophin releasing hormone; ATC code: H01CC01.

Mechanism of action

Ganirelix-AFT is a gonadotrophin-releasing hormone (GnRH) antagonist, which modulates the hypothalamic-pituitary-gonadal axis by competitive binding to the GnRH receptors in the pituitary gland. As a result a rapid, profound, reversible suppression of endogenous gonadotrophins occurs, without initial stimulation as induced by GnRH agonists.

Clinical trials

Following administration of multiple doses of 0.25 mg ganirelix to female volunteers, serum LH, FSH and E2 concentrations were maximally decreased by 74%, 32% and 25% at 4, 16 and 16 hours after injection, respectively. Serum hormone levels returned to pre-treatment values within two days after the last injection.

In patients undergoing controlled ovarian stimulation the median duration of ganirelix treatment was 5 days. During ganirelix treatment the average incidence of LH rises (>10 IU/l) with concomitant progesterone rise (>1 ng/ml) was 1.2% compared to 0.8% during GnRH agonist treatment. Early LH rises, prior to the start of ganirelix at day 6 of stimulation, did occur especially in high responders, but did not affect the clinical

outcome. In these patients LH production was rapidly suppressed after the first ganirelix administration.

In controlled studies of ganirelix, using a long protocol of GnRH agonist as a reference, treatment with the ganirelix regimen resulted in a faster follicular growth during the first days of stimulation, but the final cohort of growing follicles was slightly smaller and produced on average less oestradiol. This different pattern of follicular growth requires that FSH dose adjustments are based on the number and size of growing follicles, rather than on the amount of circulating estradiol.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

After a single subcutaneous administration of 0.25 mg, serum levels of ganirelix rise rapidly and reach peak levels (C_{max}) of approximately 15 ng/ml within 1 to 2 hours (t_{max}).

Pharmacokinetic parameters after multiple subcutaneous dosing of ganirelix (once daily injection) were similar to those after a single subcutaneous dose. After repeated dosing 0.25 mg/day steady-state levels of approximately 0.6 ng/ml were reached within 2 to 3 days.

The bioavailability of ganirelix following subcutaneous administration is approximately 91%.

Distribution

Pharmacokinetic analysis indicates an inverse relationship between bodyweight and serum concentrations of ganirelix.

Biotransformation

The major circulating component in plasma is ganirelix. Ganirelix is also the main compound found in urine. Faeces contained only metabolites. The metabolites are small peptide fragments formed by enzymatic hydrolysis of ganirelix at restricted sites. The metabolite profile of ganirelix in humans was similar to that found in animals.

Elimination

After a single subcutaneous administration of 0.25 mg, the elimination half-life ($t_{½}$) is approximately 13 hours and clearance is approximately 2.4 L/h. Excretion occurs via faeces (approximately 75%) and urine (approximately 22%).

5.3 PRECLINICAL SAFETY DATA

Preclinical data reveal no special hazard for humans based on safety pharmacology, repeated dose toxicity and genotoxicity.

Reproduction studies carried out with ganirelix at doses of 0.1 to 10 µg/kg/day subcutaneously in the rat and 0.1 to 50 µg/kg/day subcutaneously in the rabbit showed increased litter resorption in the highest dose groups. No teratogenic effects were observed.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Ganirelix-AFT solution for injection also contains glacial acetic acid, mannitol and water for injection. The pH may have been adjusted with sodium hydroxide and/or acetic acid.

6.2 INCOMPATIBILITIES

In the absence of incompatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 SHELF LIFE

24 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25 °C. Do not freeze as the syringe may break.

6.5 NATURE AND CONTENTS OF CONTAINER

Ganirelix-AFT is supplied in disposable prefilled syringes (Type I glass), containing 250 µg ganirelix/0.5 mL. The needle shield of Ganirelix-AFT contains elastomer and rubber piston contains bromobutyl rubber which come into contact with this product and may cause allergic reactions.

One box of Ganirelix-AFT contains one syringe.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

This product is for single use only. Discard any remaining contents.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

Prescription only medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

9 October 2025