AUSTRALIAN PRODUCT INFORMATION – LUVERIS® (lutropin alfa (rch))

1 NAME OF THE MEDICINE

Lutropin alfa (rch)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Lutropin alfa is a recombinant human luteinising hormone (r-hLH) derived from a Chinese Hamster Ovary cell line that has been modified by the addition of human genes encoding the LH α- and β-chains.

Each vial of LUVERIS contains 75 IU of lutropin alfa as lyophilised powder.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Powder for injection in vial(s).

LUVERIS is available as a sterile, lyophilised powder.

It is intended for co-administration with follitropin alfa as subcutaneous injection after reconstitution with sterile water for injections.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

LUVERIS in association with a recombinant follicle stimulating hormone (FSH) preparation is indicated for the stimulation of follicular development in women with severe LH and FSH deficiency.

4.2 DOSE AND METHOD OF ADMINISTRATION

Treatment with LUVERIS should be initiated under the supervision of a physician experienced in the treatment of fertility problems. Self-administration of LUVERIS should only be performed by patients who are well-motivated, adequately trained and with access to expert advice.

In LH and FSH deficient women, the objective of LUVERIS therapy, in association with FSH, is to promote follicular development followed by final maturation after the administration of human chorionic gonadotrophin (hCG). LUVERIS should be given as a course of daily injections concomitantly with FSH. If the patient is amenorrhoeic and has low endogenous oestrogen secretion, treatment can commence at any time. Nevertheless, the possibility of pregnancy should be first excluded by clinical or other means.

All clinical experience to date with LUVERIS in this indication has been gained with concomitant daily administration of follitropin alfa.

LUVERIS is intended for daily subcutaneous administration. The powder should be reconstituted, immediately prior to use, with the solvent provided.

The majority of the women with very low LH levels (< 1.2 IU/L as used in clinical studies, but this may vary from laboratory to laboratory) will have a poor ovarian response to r-hFSH alone. However, some women may have adequate follicular response. Clinicians will need to decide on a case by case basis whether to commence ovulation induction with r-hFSH alone or in combination with LUVERIS.

The efficacy studies have suggested that the minimum effective dose of LUVERIS is 37.5 IU. However, dose titration is recommended according to individual patient response.

A recommended regimen commences at 75 IU of LUVERIS daily with 75-150 IU FSH. Treatment should be tailored to the individual patient's response as assessed by measuring (i) follicle size by ultrasound and (ii) oestrogen response.

Clinical studies have employed doses of up to 225 IU of lutropin alfa and 150 IU follitropin alfa per day to induce follicular development. If a patient fails to respond after 3 weeks of treatment, the cycle should be abandoned and the patient should recommence treatment with a higher starting dose of follitropin alfa and/or LUVERIS than in the abandoned cycle.

If there is insufficient follicular growth, it is reasonable to increase the FSH dose, but if there is good follicular development with a low oestradiol level, this suggests that more LH may be required.

In clinical trials, LUVERIS has been associated with higher oestradiol levels than follitropin alfa alone. If an FSH dose increase is deemed appropriate, dose adaptation should preferably be at 7 to 14-day intervals and preferably with 37.5 to 75 IU increments.

When an optimal response is obtained, a single injection of 250 microgram of recombinant hCG (r-hCG) or 5,000 IU to 10,000 IU hCG should be administered 24 to 48 hours after the last LUVERIS and FSH injections. The patient is recommended to have coitus on the day of, and on the day following, hCG administration. Alternatively, intrauterine insemination (IUI) or another medically assisted reproduction procedure may be performed based on the physician's judgement of the clinical case.

Luteal phase support should be considered since lack of endogenous gonadotrophins after ovulation may lead to premature failure of the corpus luteum.

If an excessive response is obtained, treatment should be stopped and hCG withheld. Treatment should recommence in the next cycle at an FSH dosage lower than that of the previous cycle.

Product is for single use in one patient only. Discard any residue.

4.3 CONTRAINDICATIONS

LUVERIS is contraindicated in patients with:

- hypersensitivity to gonadotrophins or to any of the excipients
- ovarian, uterine or mammary carcinoma

- active, untreated tumours of the hypothalamus or pituitary gland
- ovarian enlargement or cyst of unknown aetiology
- gynaecological haemorrhages of unknown origin
- pregnancy and lactation

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Before starting treatment, the couple's infertility should be assessed as appropriate and putative contraindications for pregnancy evaluated. It is recommended that LUVERIS is not used in conditions where an effective response is usually not expected, such as primary ovarian failure, malformation of the sexual organs or fibroid tumours of the uterus that are incompatible with pregnancy. In addition, patients should be evaluated for hypothyroidism, adrenocortical deficiency and hyperprolactinemia, and appropriate specific treatment given.

Ovarian Hyperstimulation Syndrome (OHSS)

A certain degree of ovarian enlargement is an expected effect of controlled ovarian stimulation. It is more commonly seen in women with polycystic ovarian syndrome and usually regresses without treatment.

Distinct from uncomplicated ovarian enlargement, OHSS is a condition that can manifest itself with increasing degrees of severity. It comprises marked ovarian enlargement, high serum sex steroids, and an increase in vascular permeability which can result in an accumulation of fluid in the peritoneal, pleural and, rarely, in the pericardial cavities.

Mild to moderate OHSS is a common adverse effect of ovulation induction with gonadotrophins; the risk should be considered and discussed with women prior to treatment.

Independent risk factors for developing OHSS include young age, lean body mass, polycystic ovarian syndrome, higher doses of exogenous gonadotrophins, high absolute or rapidly rising serum oestradiol levels and previous episodes of OHSS, large number of developing ovarian follicles and large number of oocytes retrieved in Assisted Reproductive Technology (ART) cycles.

Adherence to recommended LUVERIS and FSH dosage and regimen of administration can minimise the risk of ovarian hyperstimulation. Monitoring of stimulation cycles by ultrasound scans, as well as oestradiol measurements, is recommended to identify risk factors early.

There is evidence to suggest that hCG plays a key role in triggering OHSS and that the syndrome may be more severe and more protracted if pregnancy occurs. Therefore, if monitoring results indicate a high risk of OHSS or if signs of OHSS occur, it is recommended that hCG be withheld and the patient be advised to refrain from coitus or use barrier methods of contraception for at least 4 days. As OHSS may progress rapidly (within 24 hours) or over several days to become a serious medical event, patients should be followed for at least two weeks after hCG administration.

Mild manifestations of OHSS may include abdominal pain, abdominal discomfort and distension, or enlarged ovaries. Moderate OHSS may additionally present with nausea, vomiting,

ultrasound evidence of ascites or marked ovarian enlargement. Severe OHSS further includes symptoms such as severe ovarian enlargement, weight gain, dyspnoea or oliguria. Clinical evaluation may reveal signs such as hypovolaemia, haemoconcentration, electrolyte imbalances, ascites, pleural effusions, or acute pulmonary distress. Very rarely, severe OHSS may be complicated by ovarian torsion or thromboembolic events, such as pulmonary embolism, ischaemic stroke or myocardial infarction.

Mild or moderate OHSS usually resolves spontaneously. If severe OHSS occurs, it is recommended that gonadotrophin treatment be stopped, the patient be hospitalised and appropriate therapy be started.

Multiple pregnancy

In patients undergoing induction of ovulation, the incidence of multiple pregnancy is increased compared with natural conception. The majority of multiple conceptions are twins. Multiple pregnancies, especially higher order, carry an increased risk of adverse maternal and perinatal outcomes. The patient should be advised of the potential risk of multiple births before starting treatment.

To minimise the risk of twins or higher order multiple pregnancy, careful monitoring of ovarian response is recommended. Appropriate management, such as cycle cancellation, should be considered in line with current clinical practice.

In patients undergoing ART procedures, the risk of multiple pregnancy is related mainly to the number of embryos replaced, their quality and the patient's age. Single embryo transfer in good prognosis cycles substantially reduces the risk of multiple pregnancy with little effect on live birth rates.

Pregnancy loss

The incidence of pregnancy loss by miscarriage or abortion is higher in patients undergoing stimulation of follicular growth for ovulation induction than following natural conception.

Thromboembolic events

In women with recent or ongoing thromboembolic disease or women with generally recognised risk factors for thromboembolic events, such as personal or family history, treatment with gonadotrophins may further increase the risk for aggravation or occurrence of such events. In these women, the benefits of gonadotrophin administration need to be weighed against the risks. It should be noted however, that pregnancy itself as well as OHSS also carry an increased risk of thromboembolic events.

Porphyria

In patients with porphyria or a family history of porphyria, gonadotrophins may increase the risk of an acute attack. Deterioration or a first appearance of this condition may require cessation of treatment.

Congenital anomalies

The prevalence of congenital anomalies after the use of ART may be slightly higher than after spontaneous conceptions. Possible contributing factors include aspects inherent in the couple's

infertility, ovulation induction agents, other medicines used in treatment and the ART procedures. While there is no specific evidence from clinical trials or post-marketing data implicating gonadotrophin use in adverse effects on pregnancy, embryonal or foetal development, parturition or postnatal development, ovulation induction agents cannot be excluded as a contributing factor.

Use in hepatic or renal impairment

Caution should be used, and close monitoring considered when administering LUVERIS to patients with renal or hepatic impairment. There are currently no data available on the use of LUVERIS in patients with hepatic or renal impairment.

Use in the elderly

No data available

Paediatric use

No data available

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

LUVERIS should not be administered as a mixture with other medicines in the same injection, except follitropin alfa for which studies have shown that co-administration does not significantly alter the activity, stability, pharmacokinetic nor pharmacodynamic properties of the active substances.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

See Section 4.1 THERAPEUTIC INDICATIONS

Use in pregnancy – Pregnancy Category B3

LUVERIS should not be administered during pregnancy as it may cause foetal harm when given to a pregnant woman (see Section 4.3 CONTRAINDICATIONS). Data on a limited number of human pregnancies exposed inadvertently following controlled ovarian stimulation indicate no adverse reactions of gonadotrophins on pregnancy, embryonal or foetal development, parturition or postnatal development. In the case of inadvertent administration during pregnancy, clinical data are not sufficient to exclude a teratogenic effect of LUVERIS.

Treatment of pregnant rats and rabbits with LUVERIS at doses of 10 IU/kg/day SC and above was associated with embryonic resorptions (approximately 0.4x and 0.8x clinical exposure at the maximum recommended clinical dose of 225 IU/day, based on body surface area, respectively). Teratogenicity was not observed in pregnant rats and rabbits dosed with LUVERIS at doses up to 20 IU/kg/day SC (approximately 0.8x and 1.6x clinical exposure, based on body surface area, respectively). Administration of 10 IU/kg/day LUVERIS to rats from late gestation to weaning resulted in adverse effects on the post-natal survival and growth of offspring.

Use in lactation

LUVERIS should not be administered during lactation (see Section 4.3 CONTRAINDICATIONS). Secretion of r-hLH and/or its degradation products has been shown to occur in lactating rats.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects on the ability to drive and use machines have been performed.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

LUVERIS is used for the stimulation of follicular development in association with follitropin alfa. In this context, undesirable effects may be due to either or both of the substances used, or to their pharmacodynamic consequences.

There is considerable post-marketing safety experience with human luteinising hormone (hLH) containing products of urinary origin. The safety profile of LUVERIS is expected to be very similar to that of urine derived hLH, with the exception of hypersensitivity reactions and application site disorders.

In clinical trials, a maximal score of all mild and moderate injection site reactions (bruising, pain, redness, itching or swelling) was reported in 12.7% (mild) and 2.7% (moderate) of the 2282 injections in 271 treatment cycles, respectively. Among the 170 patients treated, only 2 patients (1.2%) reported a severe injection site reaction.

OHSS was observed in 3.9% of treatment cycles with LUVERIS. Six serious OHSS reports (2.3%) occurred in 259 treatment cycles.

Ovarian cysts and enlargement are common. Complications including adnexal torsion and haemoperitoneum have been reported rarely with human menopausal gonadotrophin therapy.

Ectopic pregnancy may also occur, especially in women with a history of prior tubal disease.

The following definitions apply to the frequency terminology used hereafter:

Very Common	≥ 1/10
Common	≥ 1/100 to < 1/10
Uncommon	≥ 1/1,000 to < 1/100
Rare	≥ 1/10,000 to < 1/ 1,000
Very Rare	< 1/10 000

General disorders and administration site condition

Common: Injection site reactions (e.g. pain, erythema, haematoma, swelling and/or irritation at the site of injection)

Nervous system disorders

Common: Headache

Gastrointestinal disorders

Common: Nausea, vomiting, diarrhoea, abdominal pain, abdominal discomfort

Reproductive system and breast disorders

Common: Mild or moderate OHSS (including associated symptomatology), ovarian cyst, breast pain, pelvic pain

Vascular disorders

Very rare: Thromboembolism, usually associated with severe OHSS

Immune system disorders

Very rare: Mild to severe hypersensitivity reactions including anaphylactic reactions and shock

The reported undesirable effects are in agreement with those reported for other hLH containing products.

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 www.tga.gov.au/reporting-problems in Australia, or at https://nzphvc.otago.ac.nz/reporting/ in New Zealand.

4.9 OVERDOSE

The effects of overdosage of LUVERIS are unknown; nevertheless there is a possibility that OHSS may occur which is further described in PRECAUTIONS.

Single doses of up to 40,000 IU of LUVERIS have been administered to healthy female volunteers without serious adverse events and were well tolerated.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia) or 0800 764 766 (New Zealand).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Luteinising hormone binds on the ovarian theca (and granulosa) cells and testicular Leydig cells to a receptor shared with human chorionic gonadotrophin hormone (hCG). This LH/hCG transmembrane receptor is a member of the super-family of G protein-coupled receptors and it has a large extracellular domain. The *in-vitro* binding affinities of r-hLH, pituitary hLH and hCG to the LH/hCG receptor on murine Leydig tumour cells are of similar orders of magnitude.

Luteinising hormone (LH) and follicle stimulating hormone (FSH) are secreted from the anterior pituitary gland in response to gonadotropin-releasing hormone (GnRH) and play a

complementary role in follicle development and ovulation. In theca cells, LH stimulates the secretion of androgens that are transferred to granulosa cells to be converted to oestradiol (E2) by aromatase. In granulosa cells, FSH stimulates the development of ovarian follicles, while LH action is involved in follicle development, maturation and steroidogenesis.

In the stimulation of follicular development in anovulatory women deficient in LH and FSH, the primary effect resulting from administration of LUVERIS is an increase in oestradiol secretion by the follicles, the growth of which is stimulated by r-FSH.

Clinical trials

The safety and efficacy of LUVERIS have been examined in five studies for induction of ovulation in women with hypogonadotropic hypogonadism (HH).

Pivotal Studies

The safety and efficacy of LUVERIS administered subcutaneously and concomitantly with recombinant human FSH (r-hFSH) for ovulation induction in women with HH was assessed and confirmed in the following 2 international pivotal studies.

In clinical trials (studies 6253 and 21008), patients were defined by an endogenous serum LH level < 1.2 IU/L as measured in a central laboratory. However, it should be taken into account that there are variations between LH measurements performed in different laboratories.

Study 6253

Study 6253 was a Phase II randomized, open-label, dose-finding study to determine the minimal effective dose and assess the safety of LUVERIS to support r-hFSH-induced follicular development in LH and FSH deficient anovulatory women. Patients were randomized to treatment with 0, 25, 75 or 225 IU LUVERIS concomitant with 150 IU of r-hFSH for up to 3 treatment cycles. Thirty-eight patients were enrolled and treated in a total of 53 treatment cycles.

The proportion of patients who fulfilled the primary efficacy endpoint criteria (at least one follicle ≥ 17 mm; E_2 ≥ 400 pmol/L; mid-luteal phase P_4 ≥ 25 nmol/L) was related to the dose of LUVERIS, both when excessive follicular development was not included as a success (0.0%, 14.3%, 44.4% and 50.0% for treatment with 0, 25, 75 and 225 IU LUVERIS, respectively; p=0.0124) and when excessive follicular development was included as a success (0.0%, 14.3%, 66.7% and 80.0% for treatment with 0, 25, 75 and 225 IU LUVERIS, respectively; p=0.0001).

Study 21008

The safety and efficacy of LUVERIS 75 IU administered subcutaneously for induction of ovulation in women with HH and severe gonadotrophin deficiency was assessed in this Phase III double-blind, placebo-controlled, randomized trial of 39 women.

The primary efficacy parameter in this single-cycle study was follicular development as defined by: (i) at least one follicle with a mean diameter of ≥ 17 mm, (ii) pre-ovulatory serum E_2 level ≥ 109 pg/mL (400 pmol/L) and (iii) mid-luteal phase P_4 level ≥ 7.9 ng/mL (25 nmol/L). Patients with excessive follicular development or who became pregnant were considered treatment successes from the perspective of the analysis.

The efficacy results for Study 21008 are summarized in Table 1a.

Table 1a. Follicular Development Rate with *risk of* OHSS considered as a success (Population: ITT Patients)

Follicular Development	Placebo and r-hFSH (n=13) n (%)	75 IU LUVERIS and r-hFSH (n=26) n (%)	Total (n=39) n (%)	p-value[(a)]
Yes	2 (15.4)	17 (65.4)	19 (48.7)	0.006
No	11 (84.6)	9 (34.6)	20 (51.3)	

[(a)] Fisher's Exact Test

The efficacy results for the same study are also assessed when risk of OHSS is considered as an efficacy failure in Table 1b.

Table 1b. Follicular Development Rate and Ovulation with *risk of* OHSS considered as an efficacy failure (Population: ITT Patients)

Follicular Development	Placebo and r-hFSH (n=13) n (%)	75 IU LUVERIS and r-hFSH (n=26) n (%)	Total (n=39) n (%)	p-value[(a)]
Yes	1 (7.7)	11 (42.3)	12 (20.8)	0.034
No	12 (92.3)	15 (57.7)	27 (69.2)	

[(a)] Fisher's Exact Test

In studies 6253 and 21008, achievement of an adequate follicular development as the optimal well established and surrogate marker of conception was consistently found in 66.7% of patients with LH < 1.2 IU treated with FSH and 75 IU LUVERIS. This result was based on studies 6253 [66.7%] and 21008 [66.7%] and was calculated when risk of ovarian hyperstimulation syndrome (OHSS) and pregnancy outcome were considered as treatment successes. When risk of OHSS was considered as a treatment failure, adequate follicular development was found in 43.2% of patients (combined analysis of follicular development in studies 6253 and 21008).

Other Studies

The safety and efficacy of LUVERIS administered subcutaneously concomitantly with r hFSH for ovulation induction in women with HH was also investigated in 3 additional studies.

Study 6905 was a Phase II/III open-label, randomized, multicenter study to determine the minimal effective dose and assess the safety of LUVERIS administered with r-hFSH to induce follicular development in anovulatory women with HH and moderate gonadotrophin deficiency. Forty patients were enrolled and treated.

Study 7798 was a Phase III multicenter study to assess the efficacy and safety of LUVERIS administered with r-hFSH for induction of follicular development in LH and FSH deficient anovulatory women and enrolled 15 patients.

Study 8297 was a Phase III multicenter, non-comparative study to assess the efficacy and safety of LUVERIS administered with r-hFSH for induction of follicular development in LH and FSH-deficient anovulatory women and enrolled 38 patients.

Among the 170 patients with HH enrolled in the 5 LUVERIS development studies, 154 were seeking fertility and of these 127 were treated with LUVERIS. Overall 41 of 127 (32%) LUVERIS treated patients (all doses) and 31 of 100 (31%) in the LUVERIS 75 IU dose group achieved a pregnancy over a total of 205 treatment cycles.

Table 2. Summary of pregnancies in cycles of women wishing to conceive

Treatment	**Placebo or no LH**				**All r-hLH treated cycles**					
Study	GF 6253	21008	GF 6905	Total no LH	GF 6253	GF 6905	21008	GF 8927	GF 7798	Total LH
Cycles	**8**	**13**	**19**	**40**	**31**	**33**	**26**	**85**	**33**	**208**
Cycles with hCG	**2**	**3**	**15**	**20**	**17**	**30**	**13**	**64**	**28**	**152**
Clinical pregnancies[1]	**0**	**1**	**4**	**5**	**3**	**8**	**1**	**15**	**7**	**34**
Miscarriages			**1**	**1**	**1**	**1**		**1**	**2**	**5**
Pregnancy loss after 20 weeks								**1**		**1**
Live birth simple			**2**	**2**	**1**	**3**		**9**	**3**	**16**
Live birth multiple		**1 (twins with 1 NND[2])**	**1**	**2**	**1**	**3**		**4**	**2**	**10**
Lost to follow up						**1**	**1**			

[1] Clinical pregnancy was defined by an ultrasound detection of a sac with or without heartbeat activity on day 35-42 after hCG administration

[2] NND = neonatal death

No direct comparison of r-hLH and r-hFSH versus human menopausal gonadotrophin (hMG) has been performed. Comparison with historical data suggests that the ovulation rate with the combination is similar to what can be obtained with hMG.

5.2 PHARMACOKINETIC PROPERTIES

The pharmacokinetics of lutropin alfa have been studied in pituitary desensitised female volunteers from 75 IU up to 40,000 IU.

The pharmacokinetic profile of lutropin alfa is similar to that of urinary-derived hLH. Following intravenous administration, lutropin alfa is rapidly distributed with an initial half-life of approximately one hour and eliminated from the body with a terminal half-life of about 10-12 hours. The steady state volume of distribution is around 10-14 L. Lutropin alfa shows linear pharmacokinetics, as assessed by AUC, which is directly proportional to the dose administered.

Total clearance is around 2 L/h, and less than 5% of the dose is excreted in the urine. The mean residence time is approximately 5 hours.

Following subcutaneous administration, the absolute bioavailability is approximately 60%; the terminal half-life is slightly prolonged. The lutropin alfa pharmacokinetics following single and repeated administration of LUVERIS are comparable and the accumulation ratio of lutropin alfa minimal. There is no pharmacokinetic interaction with follitropin alfa when administered simultaneously.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Lutropin alfa was inactive in *in vitro* tests for gene mutation and chromosomal damage, and in an *in vivo* mouse micronucleus test.

Carcinogenicity

Long-term carcinogenicity studies have not been carried out.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sucrose, dibasic sodium phosphate dihydrate, methionine, monobasic sodium phosphate monohydrate, polysorbate 20, sodium hydroxide, phosphoric acid and sodium hydroxide for pH adjustment.

6.2 INCOMPATIBILITIES

See Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS.

6.3 SHELF LIFE

Information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG) in Australia or on Medsafe Product Detail in New Zealand. The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

The lyophilised product must be stored below 25°C. Protect from light.

The reconstituted solution must be injected immediately as it contains no antimicrobial agent.

6.5 NATURE AND CONTENTS OF CONTAINER

LUVERIS is supplied in packs of 1, 3 or 10 vials* with the corresponding number of vials containing 1 mL Water for Injections.

*Not all pack sizes are available

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Lutropin alfa is a recombinant human luteinising hormone (r-hLH). r-hLH is a human gonadotrophin hormone, composed of two non-covalently linked, non-identical protein components designated as the α- and β-subunits. It is a glycoprotein hormone with molecular weight (MW) of about 29,000 Da. The α-subunit is common to all four members of the gonadotropin hormone family. The α-subunit is formed by 92 amino acids and possesses two sites of N-linked glycosylation (Asn 52 and Asn 78). Five disulphide bonds contribute to its tertiary structure. The β-subunit, which is hormone specific, is 121 amino acids in length and possesses a single site of N-linked glycosylation (Asn 30). It contains six disulphide bridges.

The physicochemical, immunological and biological activities of r-hLH are comparable to those of human menopausal urinary-hLH (u-hLH). The main difference between u-hLH and r-hLH is that the u-hLH carbohydrate moieties are essentially capped with sulphate groups, while in r-hLH it is with sialic acid. Preclinical and clinical experience, however, indicate that this has no significant impact on the pharmacokinetic characteristics of these molecules.

CAS number

CAS-152923-57-4 (lutropin alfa); CAS-56832-30-5 (α-subunit); CAS-53664-53-2 (β subunit).

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 (Prescription Only Medicine)

8 SPONSOR

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9 DATE OF FIRST APPROVAL

24 March 2003

10 DATE OF REVISION

19 June 2024

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.1	The text related to clinical trials is placed under Pivotal Studies segment of Section 5.1
4.2	Updated the text related to the physiological action of the medicine
5.1	Reorganised the text related to clinical trials

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rch = Recombinant Chinese hamster