6295-03

REPRONEX®
(MENOTROPINS FOR INJECTION, USP)
FOR SUBCUTANEOUS INJECTION AND
INTRAMUSCULAR INJECTION

DESCRIPTION

Repronex® (menotropins for injection, USP) is a purified preparation of gonadotropins extracted from the urine of postmenopausal women. Each vial of Repronex® contains 75 International Units (IU) of follicle stimulating hormone (FSH) activity and 75 International Units (IU) of luteinizing hormone (LH) activity, respectively, plus 20 mg lactose monohydrate in a sterile, lyophilized form. The final product may contain sodium phosphate buffer (sodium phosphate tribasic and phosphoric acid). Repronex® is administered by subcutaneous or intra-muscular injection. Human Chorionic Gonadotropin (hCG), a naturally occurring hormone in postmenopausal urine, is detected in Repronex®.

Repronex® is biologically standardized for FSH and LH (ICSH) gonadotropin activities in terms of the Second International Reference Preparation for Human Menopausal Gonadotropins established in September, 1964 by the Expert Committee on Biological Standards of the World Health Organization.

Both FSH and LH are glycoproteins that are acidic and water soluble. Therapeutic class: Infertility.

CLINICAL PHARMACOLOGY

Menotropins administered for 7 to 12 days produces ovarian follicular growth in women who do not have primary ovarian failure. Treatment with menotropins in most instances results only in follicular growth and maturation. When sufficient follicular maturation has occurred, hCG must be given to induce ovulation.

PHARMACOKINETICS

Single doses of 300 IU menotropins (Menogon®, Ferring's European formulation) were administered subcutaneously (SC) and intramuscularly (IM) in a 2-period crossover study to 16 healthy female subjects while their endogenous FSH and LH were being suppressed. Serum FSH concentrations were determined. Based on the ratio of FSH C_{max} and $AUC_{0-\alpha}$, SC and IM administration of menotropins are not bioequivalent. Compared to IM administration, the SC administration of menotropins results in an increase of FSH C_{max} and $AUC_{0-\alpha}$ by 35 and 20%, respectively.

Based on two subjects who received either the highest SC or IM Repronex® dose, FSH pharmacokinetics (PK) appears to be linear up to 450 IU menotropins. The mean accumulation factors for FSH upon six doses of SC or IM 150 to 450 IU/day Repronex® are 1.6 and 1.4, respectively. Upon six doses of SC or IM 150 IU/day Repronex®, the observed serum FSH concentrations range from 1.7 to 15.9 mIU/mL and 0.5 to 10.1 mIU/mL, respectively. The FSH pharmacokinetic parameters from population modeling for these two studies are in Table 1.

Table 1. FSH Pharmacokinetic Parameters† Upon Menotropins Administration

	Single Dose‡		Multiple Dose¶	
FSH Parameter	SC	IM	SC	IM
Ka (h^{-1})	0.128 (42.1)	0.117 (21.3)	0.076 (46.3)	0.064 (63.2)
Cl/F (L/h)	0.770 (17.1)	0.94 (6.9)	1.11 (39.5)	1.44 (43.5)
V/F (L)	39.37 (14.1)	57.68 (11.4)	23.09 (8.3)	23.5 (2.5)

†mean (CV%)
‡Menogon® (Ferring's European formulation of menotropins)
¶Repronex®

Serum LH concentrations upon multiple dose SC or IM Repronex® are low and variable. No recognizable trend in the increase in serum LH concentrations from SC or IM 150 to 450 IU/day Repronex® doses was observed. After the 6th dose of SC or IM 150 IU/day Repronex®, the range of baseline corrected serum LH concentrations is 0 to 3.2 mIU/mL for both routes of administration.

Absorption

The geometric mean of FSH C_{max} and $AUC_{0-\alpha}$ upon single dose SC administration of menotropins is 5.62 mIU/mL and 385.2 mIU·h/mL, respectively; the corresponding geometric median of FSH t_{max} is 12 hours. The geometric mean of FSH C_{max} and $AUC_{0-\alpha}$ upon single dose IM administration of menotropins is 4.15 mIU/mL and 320.1 mIU·h/mL, respectively; the corresponding geometric median of FSH t_{max} is 18 hours.

Distribution

Human tissue or organ distribution of FSH and LH have not been studied for Repronex®.

Metabolism

Metabolism of FSH and LH have not been studied for Repronex® in humans.

Excretion

The mean elimination half-lives of FSH upon single dose SC and IM administration of menotropins are 53.7 and 59.2 hours, respectively.

Pediatric Populations

Repronex® is not used in pediatric populations.

Geriatric Populations

Repronex® is not used in geriatric populations.

Special Populations

The safety and efficacy of Repronex® in renal and hepatic insufficiency have not been studied.

Drug Interactions

No drug/drug interaction studies have been conducted for Repronex® in humans.

CLINICAL STUDIES

Efficacy results from a clinical trial in *in vitro* fertilization (IVF) patients and a clinical trial in ovulation induction (OI) in anovulatory and oligovulatory patients are summarized in Tables 2 and 3, respectively. Both studies were multicenter, active control, randomized, parallel group designs. In addition, all patients in both studies underwent pituitary suppression with a GnRH agonist before starting treatment with Repronex® or the control therapy. The IVF study evaluated 186 patients (125 patients received Repronex®). The patients treated with Repronex® received 225 IU Repronex® daily for 5 days. This was followed by individual titration of the dose from 75 to 450 IU daily based on ultrasound and estradiol (E_2) levels. The total duration of dosing did not exceed 12 days. The OI study evaluated 108 patients (72 patients received Repronex®). The patients treated with Repronex® received 150 IU Repronex® daily for 5 days. This was followed by individual titration of the dose from 75 to 450 IU daily based on ultrasound and estradiol (E_2) levels. The total duration of dosing did not exceed 12 days.

Table 2. Efficacy Outcomes by Treatment Group for IVF (one cycle of treatment)

Parameter	Repronex® IM	Repronex® SC
	N=65	N=60
Total oocytes Retrieved	13.6	12.7
Mature oocytes Retrieved	9.4	8.6
Patients with oocyte Retrieval (%)	61 (93.8)	55 (91.7)
Patients with Embryo Transfer (%)	58 (89.2)	51 (85.0)
Patients with Chemical Pregnancy (%)	31 (47.7)	35 (58.3)
Patients with Clinical Pregnancy (%)	25 (38.5)	30 (50.0)
Patients with Continuing Pregnancy (%)	24 (36.9)[1.]	29 (48.3)[2.]
Patients with Live Births (%)	22 (33.8)[3.]	25 (41.7)[4.]

1. Continuing pregnancies included 14 single, 7 twins, and 3 triplet pregnancies.
2. Continuing pregnancies included 14 single, 9 twins, 3 triplets, and 3 quadruplet pregnancies.
3. Total of 34 live births. One spontaneous abortion. The follow-up data is not available for one patient.
4. Total of 39 live births. Two spontaneous abortions. The follow-up data is not available for two patients.

Table 3. Efficacy Outcomes by Treatment Groups in Ovulation Induction (one cycle of treatment)

Parameter	Repronex® IM	Repronex® SC
	N=36	N=36
Ovulation (%)	23 (63.9)	25 (69.4)
Received hCG (%)	25 (69.4)	27 (75.0)
Mean Peak Serum E2 (SD)	1158.5 (742.3)	1452.6* (1270.6)
Chemical Pregnancy (%)	4 (11.1)	11 (30.6)
Clinical Pregnancy (%)	4 (11.1)	6 (16.7)
Continuing Pregnancy (%)	4 (11.1)[1.]	6 (16.7)[2.]
Pts. w/Live Births (%)	4 (11.1)[3.]	4 (11.1)[4.]

* Fisher's Exact/Chi-Squared Tests – significant for Repronex® SC vs. Repronex® IM

1. Continuing pregnancies included 2 single and 2 triplet pregnancies.
2. Continuing pregnancies included 3 single, 1 twin, and 2 quadruplet pregnancies.
3. Total 6 live births.
4. Total of 6 live births. One spontaneous abortion. The follow-up data is not available for one patient.

INDICATIONS AND USAGE

Repronex®, in conjunction with hCG, is indicated for multiple follicular development (controlled ovarian stimulation) and ovulation induction in patients who have previously received pituitary suppression.

Selection of Patients

1. Before treatment with Repronex® is instituted, a thorough gynecologic and endocrinologic evaluation must be performed. Except for those patients enrolled in an *in vitro* fertilization program, this should include a hysterosalpingogram (to rule out uterine and tubal pathology) and documentation of anovulation by means of basal body temperature, serial vaginal smears, examination of cervical mucus, determination of serum (or urine) progesterone, urinary pregnanediol, and endometrial biopsy. Patients with tubal pathology should receive menotropins only if enrolled in an *in vitro* fertilization program.
2. Primary ovarian failure should be excluded by the determination of gonadotropin levels.
3. Careful examination should be made to rule out the presence of an early pregnancy.
4. Patients in late reproductive life have a greater predilection to endometrial carcinoma as well as a higher incidence of anovulatory disorders. Cervical dilation and curettage should always be done for diagnosis before starting Repronex® therapy in such patients who demonstrate abnormal uterine bleeding or other signs of endometrial abnormalities.
5. Evaluation of the husband's fertility potential should be included in the workup.

CONTRAINDICATIONS

Repronex® is contraindicated in women who have:

1. A high FSH level indicating primary ovarian failure.
2. Uncontrolled thyroid and adrenal dysfunction.
3. An organic intracranial lesion such as a pituitary tumor.
4. The presence of any cause of infertility other than anovulation unless they are candidates for *in vitro* fertilization.
5. Abnormal bleeding of undetermined origin.
6. Ovarian cysts or enlargement not due to polycystic ovary syndrome.
7. Prior hypersensitivity to menotropins.
8. Repronex® is not indicated in women who are pregnant. There are limited human data on the effects of menotropins when administered during pregnancy.

WARNINGS

Repronex® is a drug that should only be used by physicians who are thoroughly familiar with infertility problems. It is a potent gonadotropic substance capable of causing mild to severe adverse reactions in women. Gonadotropin therapy requires a certain time commitment by physicians and supportive health professionals, and its use requires the availability of appropriate monitoring facilities (see **PRECAUTIONS - Laboratory Tests**). In female patients it must be used with a great deal of care.

Overstimulation of the Ovary During Repronex® Therapy

Ovarian Enlargement: Mild to moderate uncomplicated ovarian enlargement which may be accompanied by abdominal distension and/or abdominal pain occurs in approximately 5 to 10% of those treated with Repronex® menotropins and hCG, and generally regresses without treatment within two or three weeks.

In order to minimize the hazard associated with the occasional abnormal ovarian enlargement which may occur with Repronex® hCG therapy, the lowest dose consistent with expectation of good results should be used. Careful monitoring of ovarian response can further minimize the risk of overstimulation.

If the ovaries are abnormally enlarged on the last day of Repronex® therapy, hCG should not be administered in this course of therapy; this will reduce the chances of development of the Ovarian Hyperstimulation Syndrome.

The Ovarian Hyperstimulation Syndrome (OHSS): OHSS is a medical event distinct from uncomplicated ovarian enlargement. OHSS may progress rapidly to become a serious medical event. It is characterized by an apparent dramatic increase in vascular permeability which can result in a rapid accumulation of fluid in the peritoneal cavity, thorax, and potentially, the pericardium. The early warning signs of development of OHSS are severe pelvic pain, nausea, vomiting, and weight gain. The following symptomatology has been seen with cases of OHSS: abdominal pain, abdominal distension, gastrointestinal symptoms including nausea, vomiting and diarrhea, severe ovarian enlargement, weight gain, dyspnea, and oliguria. Clinical evaluation may reveal hypovolemia, hemoconcentration, electrolyte imbalances, ascites, hemoperitoneum, pleural effusions, hydrothorax, acute pulmonary distress, and thromboembolic events (see **WARNINGS - Pulmonary and Vascular Complications**). Transient liver function test abnormalities suggestive of hepatic dysfunction, which may be accompanied by morphologic changes on liver biopsy, have been reported in association with the Ovarian Hyperstimulation Syndrome (OHSS).

OHSS occured in 3 of 125 (2.4%) Repronex® treated women during ART clinical studies. None of these cases was classified as severe. In Ovulation Induction clinical studies, 4 of 72 (5.5%) Repronex® treated women developed OHSS and of this number one case was classified as severe (1.4%). Cases of OHSS are more common, more severe and more protracted if pregnancy occurs. OHSS develops rapidly; therefore patients should be followed for at least two weeks after hCG administration. Most often, OHSS occurs after treatment has been discontinued and reaches its maximum at about seven to ten days following treatment. Usually, OHSS resolves spontaneously with the onset of menses. If there is evidence that OHSS may be developing prior to hCG administration (see **PRECAUTIONS - Laboratory Tests**), the hCG should be withheld.

If OHSS occurs, treatment should be stopped and the patient hospitalized. Treatment is primarily symptomatic, consisting of bed rest, fluid and electrolyte management, and analgesics if needed. The phenomenon of hemoconcentration associated with fluid loss into the peritoneal cavity, pleural cavity, and the pericardial cavity has been seen to occur and should be thoroughly assessed in the following manner: 1) fluid intake and output, 2) weight, 3) hematocrit, 4) serum and urinary electrolytes, 5) urine specific gravity, 6) BUN and creatinine, and 7) abdominal girth. These determinations are to be performed daily or more often if the need arises.

With OHSS there is an increased risk of injury to the ovary. The ascitic, pleural, and pericardial fluid should not be removed unless absolutely necessary to relieve symptoms such as pulmonary distress or cardiac tamponade. Pelvic examination may cause rupture of an ovarian cyst, which may result in hemoperitoneum, and should therefore be avoided. If this does occur, and if bleeding becomes such that surgery is required, the surgical treatment should be designed to control bleeding and to retain as much ovarian tissue as possible. Intercourse should be prohibited in those patients in whom significant ovarian enlargement occurs after ovulation because of the danger of hemoperitoneum resulting from ruptured ovarian cysts.

The management of OHSS may be divided into three phases: the acute, the chronic, and the resolution phases. Because the use of diuretics can accentuate the diminished intravascular volume, diuretics should be avoided except in the late phase of resolution as described below.

Acute Phase: Management during the acute phase should be designed to prevent hemoconcentration due to loss of intravascular volume to the third space and to minimize the risk of thromboembolic phenomena and kidney damage. Treatment is designed to normalize electrolytes while maintaining an acceptable but somewhat reduced intravascular volume. Full correction of the intravascular volume deficit may lead to an unacceptable increase in the amount of third space fluid accumulation. Management includes administration of limited intravenous fluids, electrolytes, and human serum albumin. Monitoring for the development of hyperkalemia is recommended.

Chronic Phase: After stabilizing the patient during the acute phase, excessive fluid accumulation in the third space should be limited by instituting severe potassium, sodium, and fluid restriction.

Resolution Phase: A fall in hematocrit and an increasing urinary output without an increased intake are observed due to the return of third space fluid to the intravascular compartment. Peripheral and/or pulmonary edema may result if the kidneys are unable to excrete third space fluid as rapidly as it is mobilized. Diuretics may be indicated during the resolution phase if necessary to combat pulmonary edema.

Pulmonary and Vascular Complications
Serious pulmonary conditions (e.g., atelectasis, acute respiratory distress syndrome) have been reported. In addition, thromboembolic events both in association with, and separate from, the Ovarian Hyperstimulation Syndrome have been reported following menotropins therapy. Intravascular thrombosis and embolism, which may originate in venous or arterial vessels, can result in reduced blood flow to critical organs or the extremities. Sequelae of such events have included venous thrombophlebitis, pulmonary embolism, pulmonary infarction, cerebral vascular occlusion (stroke), and arterial occlusion resulting in loss of limb. In rare cases, pulmonary complications and/or thromboembolic events have resulted in death.

Multiple Pregnancies
Multiple pregnancies have occurred following treatment with Repronex® IM and SC. In a clinical trial for ovulation induction in which Repronex® IM and Repronex® SC were directly compared, the rates of multiple pregnancies were as follows. Of the four clinical pregnancies with Repronex® IM, two were single and two were multiple pregnancies. Both multiple pregnancies were triplet pregnancies. Of the six clinical pregnancies with Repronex® SC, three were single and three were multiple pregnancies. The three multiple pregnancies included one twin pregnancy and two quadruplet pregnancies.

In a clinical trial of IVF patients in which Repronex® IM and Repronex® SC were directly compared, the rates of multiple pregnancies were as follows. Of the 24 continuing pregnancies on Repronex® IM, 14 were single and 10 were multiple pregnancies. The ten multiple pregnancies included three triplet and seven twin pregnancies. Of the 29 continuing pregnancies on Repronex® SC, 14 were single and 15 were multiple pregnancies. The 15 multiple pregnancies included three quadruplet, three triplet and nine twin pregnancies. The patient and her partner should be advised of the potential risk of multiple births before starting treatment.

Hypersensitivity/Anaphylactic Reactions
Hypersensitivity/anaphylactic reactions associated with menotropins administration have been reported in some patients. These reactions presented as generalized urticaria, facial edema, angioneurotic edema, and/or dyspnea suggestive of laryngeal edema. The relationship of these symptoms to uncharacterized urinary proteins is uncertain.

PRECAUTIONS
General
Careful attention should be given to diagnosis in the selection of candidates for menotropins therapy (see **INDICATIONS AND USAGE - Selection of Patients**).

Information for Patients
Prior to therapy with Repronex®, patients should be informed of the duration of treatment and the monitoring of their condition that will be required. Possible adverse reactions (see **ADVERSE REACTIONS**) and the risk of multiple births should also be discussed.

Laboratory Tests
Treatment for Induction of ovulation
The combination of both estradiol levels and ultrasonography are useful for monitoring the growth and development of follicles, timing hCG administration, as well as minimizing the risk of the Ovarian Hyperstimulation Syndrome and multiple gestation.

The clinical confirmation of ovulation, is determined by:
a) A rise in basal body temperature;
b) Increase in serum progesterone; and
c) Menstruation following the shift in basal body temperature.

When used in conjunction with indices of progesterone production, sonographic visualization of the ovaries will assist in determining if ovulation has occurred. Sonographic evidence of ovulation may include the following:
a) Fluid in the cul-de-sac;
b) Ovarian stigmata; and
c) Collapsed follicle.

Because of the subjectivity of the various tests for the determination of follicular maturation and ovulation, it cannot be overemphasized that the physician should choose tests with which he/she is thoroughly familiar.

Carcinogenesis and Mutagenesis
Long-term toxicity studies in animals have not been performed to evaluate the carcinogenic potential of menotropins.

Pregnancy
Pregnancy Category X: (see **CONTRAINDICATIONS**).

Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised if menotropins are administered to a nursing woman.

Pediatric Patients
Safety and effectiveness in pediatric patients have not been established.

Geriatric Patients
Safety and effectiveness in geriatric patients have not been established.

ADVERSE REACTIONS
The following adverse reactions, reported during menotropins therapy, are listed in decreasing order of potential severity:
1. Pulmonary and vascular complications (see **WARNINGS**)
2. Ovarian Hyperstimulation Syndrome (see **WARNINGS**)
3. Hemoperitoneum
4. Adnexal torsion (as a complication of ovarian enlargement)
5. Mild to moderate ovarian enlargement
6. Ovarian cysts
7. Abdominal pain
8. Sensitivity to menotropins (Febrile reactions suggestive of allergic response have been reported following the administration of menotropins. Reports of flu-like symptoms including fever, chills, musculoskeletal aches, joint pains, nausea, headaches, and malaise have also been reported).
9. Gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal cramps, bloating)
10. Pain, rash, swelling, and/or irritation at the site of injection
11. Body rashes
12. Dizziness, tachycardia, dyspnea, and tachypnea

The following medical events have been reported subsequent to pregnancies resulting from menotropins therapy:
1. Ectopic pregnancy
2. Congenital abnormalities

With menotropin therapy congenital abnormalities have been reported. One infant was shown to have multiple congenital anomalies consisting of aplasia of the sigmoid colon, cecovesicle fistula, bifid scrotum, meningocele, bilateral internal tibial torsion, and right metatarsus adductus. Other reported anomalies include imperforate anus, congenital heart lesions, supernumerary digits, hypospadias, extrophy of the bladder, Down's Syndrome, and hydrocephalus. The incidence of congenital abnormalities does not exceed that found in the general population.

There have been infrequent reports of ovarian neoplasms, both benign and malignant, in women who have undergone multiple drug regimens for ovulation induction; however, a causal relationship has not been established.

Adverse events occurring in ≥1% of patients exposed to Repronex® IM or Repronex® SC are described in Table 4.

Table 4: Patients with Adverse Events ≥1%

	Repronex® IM (N=101)	Repronex® SC (N=96)
Adverse Events	n (%)	n (%)
INJECTION SITE AEs		
Injection Site Edema	1 (1.0)	8 (8.3)*
Injection Site Reaction	2 (2.0)	8 (8.3)*
GENITOURINARY/REPRODUCTIVE AEs		
OHSS	2 (2.0)	5 (5.2)
Vaginal Hemorrhage	8 (7.9)	3 (3.1)
Ovarian Disease	3 (3.0)	8 (8.3)
Ectopic Pregnancy	1 (1.0)	1 (1.0)
Pelvic Pain	3 (3.0)	1 (1.0)
Breast Tenderness	2 (2.0)	2 (2.1)
GASTROINTESTINAL AEs		
Nausea	4 (4.0)	7 (7.3)
Vomiting	0 (0)	3 (3.1)
Diarrhea	0 (0)	2 (2.1)
Abdominal Cramping	7 (6.9)	5 (5.2)
Abdominal Pain	5 (5.0)	7 (7.3)
Enlarged Abdomen	6 (6.0)	2 (2.1)
OTHER BODY SYSTEM AEs		
Headache	6 (6.0)	5 (5.2)
Infection	1 (1.0)	0 (0)
Dyspnea	1 (1.0)	2 (2.1)

* Fisher's Exact/Chi-Squared Tests – significant for Repronex® SC vs. Repronex® IM.

DRUG ABUSE AND DEPENDENCE
There have been no reports of abuse or dependence with menotropins.

OVERDOSAGE
Aside from possible ovarian hyperstimulation (see **WARNINGS**), little is known concerning the consequences of acute overdosage with menotropins.

DOSAGE AND ADMINISTRATION
1. Dosage:
Infertile patients with oligo-anovulation:
The dose of Repronex® to stimulate development of ovarian follicles must be individualized for each patient. The lowest dose consistent with achieving good results based on clinical experience and reported clinical data should be used.

The recommended initial dose of Repronex® for patients who have received GnRH agonist or antagonist pituitary suppression is 150 IU daily for the first 5 days of treatment. Based on clinical monitoring (including serum estradiol levels and vaginal ultrasound results) subsequent dosing should be adjusted according to individual patient response. Adjustments in dose should not be made more frequently than once every 2 days and should not exceed more than 75 to 150 IU per adjustment. The maximum daily dose of Repronex® should not exceed 450 IU and dosing beyond 12 days is not recommended.

If patient response to Repronex® is appropriate, hCG (5,000 to 10,000 USP units) should be given 1 day following the last dose of Repronex®. The hCG should be withheld if the serum estradiol is greater than 2000 pg/mL, if the ovaries are abnormally enlarged or if abdominal pain occurs, and the patient should be advised to refrain from intercourse. These precautions may reduce the risk of Ovarian Hyperstimulation Syndrome and multiple gestation. Patients should be followed closely for at least 2 weeks after hCG administration. If there is inadequate follicle development or ovulation without subsequent pregnancy, the course of treatment with Repronex® may be repeated. The couple should be encouraged to have intercourse daily, beginning on the day prior to the administration of hCG until ovulation becomes apparent from the indices employed for the determination of progestational activity. In the light of the foregoing indices and parameters mentioned, it should become obvious that, unless a physician is willing to devote considerable time to these patients and be familiar with and conduct the necessary laboratory studies, he/she should not use Repronex®.

Assisted Reproductive Technologies:
The recommended initial dose of Repronex® for patients who have received GnRH agonist or antagonist pituitary suppression is 225 IU. Based on clinical monitoring (including serum estradiol levels and vaginal ultrasound results) subsequent dosing should be adjusted according to individual patient response. Adjustments in dose should not be made more frequently than once every 2 days and should not exceed more than 75 to 150 IU per adjustment. The maximum daily dose of Repronex® given should not exceed 450 IU and dosing beyond 12 days is not recommended.

Once adequate follicular development is evident, hCG (5,000 to 10,000 USP units) should be administered to induce final follicular maturation in preparation for oocyte retrieval. The administration of hCG must be withheld in cases where the ovaries are abnormally enlarged on the last day of therapy. This should reduce the chance of developing OHSS.

2. Administration:
Dissolve the contents of one to 6 vials of Repronex® in one to two mL of sterile saline and **ADMINISTER SUBCUTANEOUSLY OR INTRAMUSCULARLY** immediately. Any unused reconstituted material should be discarded.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

The lower abdomen (alternating sides) should be used for subcutaneous administration.

HOW SUPPLIED
Repronex® (menotropins for injection, USP) is available in vials as a sterile, lyophilized, white to off-white powder or pellet.

Each vial is available with an accompanying vial of sterile diluent containing 2 mL of 0.9% Sodium Chloride Injection, USP:

75 IU FSH and 75 IU of LH activity, supplied as:
NDC 55566-7185-2 – Box of 5 vials + 5 vials diluent

By biological assay, one IU of LH for the Second International Reference Preparation (2nd-IRP) for hMG is biologically equivalent to approximately 0.5 U of hCG.

Lyophilized powder may be stored refrigerated or at room temperature (3° to 25°C / 37° to 77°F). Protect from light. Use immediately after reconstitution. Discard unused material.

Rx only

Vials of sterile diluent of 0.9% Sodium Chloride Injection, USP manufactured for Ferring Pharmaceuticals Inc.

Manufactured for:
FERRING PHARMACEUTICALS INC.
PARSIPPANY, NJ 07054
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