



# CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

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Coverage Position Number ..... 4029

## Subject Menotropin Therapy

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Infertility Services

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

## Coverage Policy

Menotropin Therapy includes the following drugs:

- Menopur®
- Repronex®

**Note: Injectable fertility medications are specifically excluded under most CIGNA HealthCare pharmacy benefit plans. Please refer to the applicable benefit plan document to determine benefit availability and the terms and conditions of coverage.**

If coverage is available for injectable fertility medications, then:

**CIGNA covers Menotropin Therapy as medically necessary when used in combination with hCG (human Chorionic Gonadotropin) therapy for either of the following:**

- ovulation stimulation in females for either of the following:
  - as part of Assisted Reproductive Technology (ART) program
  - oligoovulatory or anovulatory infertile individuals in whom the cause of infertility is functional and not due to primary ovarian failure
- spermatogenesis stimulation in males for primary or secondary hypogonadotropic hypogonadism not due to primary testicular failure

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## **FDA Approved Indications**

### **Menopur**

Menopur administered subcutaneously is indicated for the development of multiple follicles and pregnancy in the ovulatory patients participating in an ART program.

### **Repronex**

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.

## **FDA Recommended Dosing**

Menotropins must be administered parenterally. Because absorption is greater with subcutaneous (SC) use than intramuscular (IM) use, the two routes are not bioequivalent. The distribution and metabolism of menotropins have not been studied. About 10% of the dose is excreted unchanged in the urine.

Pharmacokinetics have not been studied in special populations.

### **Menopur**

The recommended initial dose of Menopur for patients who have received a GnRH agonist for 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 two days and should not exceed 150 IU per adjustment. The maximum daily dose of Menopur given should not exceed 450 IU and dosing beyond 20 days is not recommended. Once adequate follicular development is evident, hCG should be administered to induce final follicular maturation in preparation for oocyte retrieval.

### **Repronex**

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 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.

## **Drug Availability**

### **Menopur**

Menopur is available by prescription in 5 mL vials containing 75 IU FSH and 75 IU LH activity with accompanying diluent.

### **Repronex**

Repronex is available by prescription in 5 mL vials containing 75 IU FSH and 75 LH activity with accompanying diluent.

## **General Background**

### **Pharmacology**

Menotropins are useful in anovulatory and oligoovulatory patients, patients with unexplained infertility, and patients undergoing assisted reproductive technology programs (i.e., in vitro fertilization [IVF] or intracytoplasmic sperm injection). These agents are typically used together with gonadotropin-releasing hormone (GnRH) agonists to suppress the pituitary gland and prevent premature ovulation. Menotropins are used in combination with human chorionic gonadotropin (hCG) to induce ovulation in anovulatory females without primary ovarian failure, stimulate follicular development in ovulatory females undergoing IFV, and stimulate spermatogenesis in males with hypogonadotropic hypogonadism.

Menotropins are a purified gonadotropin preparation obtained from the urine of postmenopausal women. Menotropins are biologically standardized for hormonal activity, providing one international unit (IU) of follicle-stimulating hormone (FSH) activity for each one IU of luteinizing hormone (LH) activity. Menotropins provide the pharmacologic activity of both FSH and LH. In women without primary ovarian failure, the FSH effects are dominant, stimulating growth and maturation of ovarian follicles. Additional LH must be given, as hCG, to induce ovulation after follicular maturation. In men with pituitary hypofunction, menotropins exert primarily LH effects and induce spermatogenesis.

### Clinical Efficacy

Menotropins and follitropins have been compared in both in-vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) patients and polycystic ovary syndrome (PCOS) patients. Follitropins are another type of gonadotropin used to stimulate ovulation. In IVF/ICSI patients, pregnancy rates per cycle tend to be slightly higher with follitropins than menotropins. The treatment effect is greatest when GnRH agonists are not used. However, there is no efficacy difference when GnRH agonists are used. In PCOS patients, the two agents produce equivalent pregnancy rates, although the risk of ovarian hyperstimulation syndrome (OHSS) is lower with follitropins. Comparative trials between the two available brands of menotropins are lacking.

### Adverse Reactions/Contraindications

The most common side effects in women are uncomplicated ovarian enlargement, nonspecific ovarian disease, vaginal hemorrhage, abdominal pain or cramping, enlarged abdomen, headache, and nausea. Severe adverse reactions may occur and include pulmonary complications, thromboembolic events, OHSS, hemoperitoneum, and torsion of the ovaries, uterine ligaments, or uterine tubes. Injection site reactions are more common with SC than IM administration. Drug interaction studies have not been conducted.

Menotropins are contraindicated in women who exhibit: a high FSH level indicating primary ovarian failure; uncontrolled thyroid or adrenal dysfunction; an organic intracranial lesion such as pituitary tumor; sex hormone-dependent tumors of the reproductive tract and accessory organs; causes of infertility other than anovulation unless they are candidates for IVF; abnormal uterine bleeding of undetermined origin; ovarian cysts or enlargement not due to polycystic ovary syndrome; prior hypersensitivity to menotropins; or pregnancy.

## Coding/Billing Information

**Note:** This list of codes may not be all-inclusive.

**If benefit coverage is available for injectable fertility medications under the Pharmacy Benefit plan, the following may be considered for coverage:**

HCPCS Codes	Description
S0122	Injection, Menotropins , 75 IU

ICD-9-CM Diagnosis Codes	Description
256.8	Other ovarian dysfunction
257.2	Other testicular hypofunction
628.0	Female infertility associated with anovulation

## References

1. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists number 34, February 2002. Management of infertility caused by ovulatory dysfunction. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2002; 99:347-358.

2. Ferring Pharmaceuticals, Inc. Menopur (menotropins for subcutaneous injection) package insert. Suffern, NY: Ferring Pharmaceuticals, Inc. March 2006.
3. Ferring Pharmaceuticals, Inc. Repronex (Menotropins for subcutaneous and intramuscular injection) package insert. Suffern, NY: Ferring Pharmaceuticals, Inc. March 2003.
4. McEvoy GK, ed. AHFS 2010 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2010.
5. Speroff L, Glass RH, Kase NG, editors. Clinical Gynecologic Endocrinology and Infertility 6th ed. Baltimore, MD: Lippincott Williams and Wilkins, 1999.
6. Strehler E, Abt M, El-Danasouri I, De Santo M, Sterzik K. Impact of recombinant follicle-stimulating hormone and human menopausal gonadotropins on in vitro fertilization outcome. Fertil Steril 2001; 75:332-6.
7. Westergaard LG, Erb K, Laursen SB, Rex S, Rasmussen PE. Human menopausal gonadotropin versus recombinant follicle-stimulating hormone in normogonadotropic women down-regulated with a gonadotropin-releasing hormone agonist who were undergoing in vitro fertilization and intracytoplasmic sperm injection: a prospective randomized study. Fertil Steril 2001; 76:543-9.

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