UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 1143-11
Program	Prior Authorization/Notification
Medication	Menopur® (menotropins) *
P&T Approval Date	8/2014, 5/2015, 5/2016, 5/2017, 5/2018, 5/2019, 5/2020, 6/2021, 6/2022, 6/2023, 6/2024
Effective Date	9/1/2024

1. **Background:**

The body produces two types of gonadotropins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), both of which play a role in fertility and human reproduction. After they are produced by the pituitary gland, gonadotropins trigger production of other sex hormones which then promote production of egg and sperm. Gonadotropins include hMG (human menopausal gonadotropin –Menopur) and follicle stimulating hormone. Gonadotropins are used in the treatment of infertility, a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse or therapeutic donor insemination.[1,2]

Menopur (menotropins) is indicated for the development of multiple follicles and pregnancy in ovulatory women participating in an assisted reproductive technology (ART) program.[3] hMG is used for the treatment of ovulation induction in women with ovulatory dysfunction including polycystic ovary syndrome (PCOS) who failed on clomiphene as well as for ovulation induction in the setting of hypogonadotropic hypogonadism. hMG is also used for induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure.[4-14]

The clinically appropriate dosing for hMG agents when used in an ART cycle without an FSH product is 450 IU/day or less for not more than 14 days of treatment. When used as part of a mixed stimulation protocol (hMG + FSH) or when used alone for ovulation induction or ovarian stimulation the clinically appropriate maximum dosing for hMG agents is 225 IU/day and 150 IU/day, respectively. Exceeding this daily dose and duration of treatment has not been proven to be efficacious in terms of pregnancy outcome.[9,13,14]

2. Coverage Criteria[a]:

A. <u>Ovarian Stimulation</u>

1. **Menopur** will be approved based on **<u>one</u>** of the following criteria*ǂ **:**

   a. **All** of the following:

      (1) Diagnosis of infertility

      -AND-

      (2) For the development of multiple follicles (ovarian stimulation)

-AND-

(3) **One** of the following:

(a) **Both** of the following:

i. **One** of the following exists:
- Diminished ovarian reserve
- Endometriosis
- Male factor infertility
- Tubal factor infertility
- Unexplained infertility
- Uterine infertility
- Ovulatory dysfunction
- Recurrent pregnancy loss
- Failure to achieve conception with other treatment modalities

-AND-

ii. Will be used in conjunction with assisted reproductive technology (ART)

-OR-

(b) **Both** of the following:

i. **One** of the following exists:

- Diminished ovarian reserve
- Mild to moderate male factor infertility
- Minimal to mild endometriosis
- Unilateral tubal factor infertility
- Unexplained infertility

-AND-

ii. Will be used in conjunction with intrauterine insemination (IUI)

-OR-

b. **All** of the following:

(1) Used for fertility preservation

-AND-

(2) The individual will undergo at least one of the following that would be associated with causing a primary ovarian insufficiency, infertility, or sterility:

(a) Exposure to cytotoxic agents [e.g., Cytoxan (cyclophosphamide),

procarbazine, vinblastine, cisplatin]
(b) Radiation therapy
(c) Invasive surgery

-AND-

(3) Will be used as part of an assisted reproductive technology (e.g., in vitro fertilization) procedure

Authorization will be issued for 2 months.§

B. <u>Ovulation Induction (Off-Label)</u>

1. **Menopur** will be approved based on **<u>all</u>** of the following criteria*ǂ **:**

a. Diagnosis of ovulatory dysfunction

-AND-

b. **<u>One</u>** of the following exists:

(1) Anovulation
(2) Oligo-ovulation
(3) Amenorrhea

-AND-

c. Other specific causative factors (e.g., thyroid disease, hyperprolactinemia) have been excluded or treated

-AND-

d. Infertility is not due to primary ovarian failure

-AND-

e. For induction of ovulation

Authorization will be issued for 2 months.§

C. <u>Male Hypogonadotropic Hypogonadism</u>

1. **Menopur** will be approved based on **<u>all</u>** of the following criteria*ǂ**:**

a. **<u>One</u>** of the following:

(1) Diagnosis of male primary hypogonadotropic hypogonadism

-OR-

(2) Diagnosis of male secondary hypogonadotropic hypogonadism

-AND-

b. For induction of spermatogenesis

-AND-

c. Infertility is not due to primary testicular failure

Authorization will be issued for 2 months.§

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Programs:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

*Infertility is typically excluded from coverage for UnitedHealthcare. Please refer to member's specific benefits for coverage determination.

ǂ OptumHealth review only: Please refer to the Clinical Policy on Human Menopausal Gonadotropin (hMG) Used in the Treatment of Infertility for state-specific requirements that may apply.

§ OptumHealth review only: Subsequent authorizations will be reviewed according to the Infertility Clinical Performance Guideline.

4. References:

1. World Health Organization web site. https://www.who.int/health-topics/infertility#tab=tab Accessed May 3, 2024.
2. American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: a committee opinion. Fertil Steril 2013;Jan;99(1):63.
3. Menopur [package insert]. Parsippany, NJ: Ferring Pharmaceuticals, Inc.; May 2018.
4. Platteau P, Andersen AN, Balen A, et al. Similar ovulation rates, but different follicular development with highly purified menotrophin compared with recombinant FSH in WHO Group II anovulatory infertility: a randomized controlled study. Hum. Reprod. 2006;21:1798-1804.
5. Kelly AC, Jewlewicz R. Alternate regimens for ovulation induction in polycystic ovarian disease. Fertil Steril. 1990;54;195-202.
6. Muasher SJ. Use of gonadotrophin-releasing hormone agonists in controlled ovarian hyperstimulation for in vitro fertilization. Clin Ther 1992;14(Suppl A):74-86.

7. Ferraretti A, Marca A, Fauser B, et al. ESHRE consensus on the definition of 'poor response' to ovarian stimulation for in vitro fertilization: the Bologna criteria. Human Reprod 2011; 26: 1616-24.
8. Andoh K, Mizunuma H, Liu X, et al. A comparative study of fixed-dose, stepdown, and low-dose step-up regimens of human menopausal gonadotropin for patients with polycystic ovary syndrome. Fertil Steril m1998: 70; 840-846.
9. Pal L, Jindal S, Witt B, Santoro N. Less is more: increased gonadotropin use for ovarian stimulation adversely influences clinical pregnancy and live birth after in vitro fertilization. Fertil Steril 2008;89:1694-701.
10. Fauser B, Nargund G, Anderson A, et al. Mild ovarian stimulation for IVF: 10 years later. Human Reprod 2010; 25: 2678-84.
11. Baart E, Martini E, Eijkemans M, et al. Milder ovarian stimulation for in-vitro fertilization reduces aneuploidy in the human preimplantation embryo: a randomized controlled trial. Human Reprod 2007; 22: 980-8.
12. Sunkara S, Rittenberg V, Raine-Fenning N, et al. Association between the number of eggs and live birth in IVF treatment: an analysis of 400,135 treatment cycles. Human Reprod 2011; 26: 1768-74.
13. The Practice Committee of the American Society for Reproductive Medicine. Use of exogenous gonadotropins in anovulatory women: a technical bulletin. Fertil Steril 2008;90:S7–12.
14. Practice Committees of the American Society for Reproductive Medicine and Society for Reproductive Endocrinology and Infertility. Electronic address: asrm@asrm.org. Use of exogenous gonadotropins for ovulation induction in anovulatory women: a committee opinion. Fertil Steril. 2020;113(1):66-70. doi:10.1016/j.fertnstert.2019.09.020

Program	Prior Authorization/Notification - Menopur (menotropins),
Change Control	
8/2014	Separated Gonadotropin Notification into individual documents. Removed Repronex because it has been discontinued by the manufacturer. Revised criteria for controlled ovarian stimulation and ovulation induction. Updated background and references.
5/2015	Added Repronex to program since still being manufactured. Minor change to criteria. Updated background and references.
5/2016	Annual review. Updated criteria for controlled ovarian stimulation. Updated background and references.
5/2017	Annual review. Removed Repronex because it has been discontinued by the manufacturer. Updated background and references.
5/2018	Annual review. No changes to criteria. Updated references.
5/2019	Annual review. No changes to criteria. Updated references.
5/2020	Annual review. No changes to coverage criteria.
6/2021	Annual review. No changes to criteria. Updated references.
6/2022	Annual review. Updated references.
6/2023	Annual review. Clarified that criteria for induction of spermatogenesis are specific to male hypogonadotropic hypogonadism. Removed broken hyperlink to Infertility Clinical Performance Guideline. Updated background, added state mandate, and updated references.
6/2024	Annual review. Added coverage criteria for fertility preservation for iatrogenic infertility. Updated term "controlled ovarian stimulation" to "ovarian stimulation". Updated references.