

Fertility Drugs and Vaginal Progesterone

To Initiate a Coverage Review, call 1 800 753-2851

Covered Medications

- Clomiphene Citrate (*Clomid*[®], *Serophene*[®])
- Gonadotropins:
 - Menotropins (*Pergonal*[®], *Humegon*[®], *Repronex*[®])
 - Urofollitropin (*Fertinex*[®], *Bravelle*[®])
 - Follitropin alfa (*Gonal-F*[®], *Gonal-F*[®] pen)
 - Follitropin beta (*Follistim*[®], *Follistim*[®] AQ)
 - Lutropin alfa (*Luveris*[®])
- Human Chorionic Gonadotropin (*Profasi HP*[®], *A.P.L.*[®], *Chorex-5*[®], *Chorex-10*[®], *Choron 10*[®], *Gonic*[®], *Pregnyl*[®], *Novarel*[®], *Ovidrel*[®])
- Synthetic Gonadotropin Releasing Hormone; Gonadorelin (*Factrel*[®], *Lutrepulse*[®])
- Gonadotropin Releasing Hormone Agonist; Leuprolide (*Lupron*[®]), Nafarelin (*Synarel*[®])
- Gonadotropin Releasing Hormone Antagonist; Ganirelix (formerly *Antagon*[®]), Cetrorelix (*Cetrotide*[®])
- Vaginal Progesterone (*Crinone*[®], *Endometrin*[®] and *Prochieve*[®])

What They Do and How They Are Used

- Infertility affects 15% of couples. Problems with female reproduction accounts for 40% of the causes of infertility. In most cases, drug therapy is aimed at correcting or enhancing a female's reproductive capability. A couple is considered infertile if they are unable to conceive after 6 to 12 months of unprotected intercourse.
- Drug therapy is administered in treatment cycles. The start of a cycle is considered to be when a woman starts taking drugs to stimulate oocyte (egg) production or starts ovarian monitoring with the intent of having embryos transferred. A woman's fertility cycle (menstrual cycle) can range from 28 to 35 days and occurs approximately once per month. It is divided into two phases with the follicular phase beginning from the first day of menses (day 1) and lasting until day 14, followed by the luteal phase which lasts until the next menstrual period.
- During the follicular phase, oocytes are forming to be released with the onset of the luteal phase which prepares the endometrium to support a mature oocyte.
- Clomiphene is typically used first line before other drugs in some circumstances. It indirectly stimulates ovulation and enhances the normal menstrual cycle. Clomiphene may be administered for 5 days starting on the fifth day of the cycle.
- Menotropins, urofollitropins and follitropins are collectively known as gonadotropins. Most gonadotropins contain two hormones, follicle stimulating hormone (FSH) and luteinizing hormone (LH), which control ovulation in women. Lutropin alfa (*Luveris*[®]) is the only gonadotropin that contains only luteinizing hormone. The woman's body must produce these hormones in the proper sequence and the right amounts as an imbalance in the production of either hormone drastically reduces the chance for conception. For products containing both FSH and LH, the ratio of FSH to LH differs based on the specific gonadotropin. Menotropins contain a 1:1 ratio of FSH and LH, whereas urofollitropins and follitropins contain mainly FSH. These drugs are given for 5 – 12 days to stimulate the growth of follicles (FSH mediated) and/or to stimulate the follicle to release the egg (LH mediated).
- Human chorionic gonadotropin (HCG) is given 1 day following the last dose of gonadotropin to facilitate the release of the mature egg from the ovaries.
- Gonadotropin releasing hormone agonists are given every day to decrease the endogenous levels of LH and FSH thereby preventing the release of the eggs before they are ready for fertilization. This treatment is known as controlled ovarian stimulation.
- Gonadotropin releasing hormone (GnRH) antagonists have the same function as GnRH agonists but may be administered for a shorter duration (e.g., up to 10 days).
- Synthetic GnRH stimulates the release of LH to induce ovulation. It aids infertility treatment in women with polycystic ovaries.
- Progesterone is a naturally occurring steroid that is secreted by the ovary, placenta and adrenal gland. It is required to prepare the lining of the uterus (endometrium) to receive and nourish an embryo during pregnancy.

- Progesterone gel may be administered for progesterone supplementation or replacement adjunctively in the treatment of infertility in progesterone deficient women.
- Progesterone gel may be used to prevent spontaneous abortion in women with luteal phase deficient progesterone production.
- Progesterone may be used as a component of hormonal replacement regimens containing estrogen and progestins.

Drugs	Use for Conditions Other than Infertility
Clomiphene	<ul style="list-style-type: none"> ▪ Administered as a first line regimen to evaluate a female's candidacy for infertility treatment ▪ Amenorrhea (absence of menstrual cycle)
Gonadotropins	<ul style="list-style-type: none"> ▪ Hypogonadotropic hypogonadism (low levels of sex hormones) ▪ Hypopituitarism (decreased production of growth hormones from the pituitary gland)
HCG	<ul style="list-style-type: none"> ▪ Prepubertal cryptorchidism (failure of testicular descent during puberty) ▪ Hypogonadotropic hypogonadism
Synthetic GnRH	<ul style="list-style-type: none"> ▪ Endometriosis (uterine tissue overgrowth)
GnRH Agonists	<ul style="list-style-type: none"> ▪ Central precocious puberty ▪ Endometriosis ▪ Uterine leiomyomata (smooth muscle tumors in the uterus) ▪ Treatment of prostate cancer
Vaginal Progesterone	<ul style="list-style-type: none"> ▪ Hormonal supplementation in women with recurrent spontaneous abortion due to luteal phase deficiency. ▪ Secondary amenorrhea or dysfunctional uterine bleeding

Rationale for Prior Authorization

Fertility Agents:

To limit coverage of fertility drugs to non-fertility uses covered by the plan and fertility uses in patients between the ages of 18 and 45 years of age who are not utilizing the medications in conjunction with Assisted Reproductive Technology (ART) procedures. ART procedures include In Vitro Fertilization (IVF), Gamete Intrafallopian Transfer (GIFT), Zygote Intrafallopian Transfer (ZIFT) and Intrauterine or Artificial Insemination.

Vaginal Progesterone:

To limit coverage to progesterone supplementation in women with recurrent spontaneous abortion due to luteal phase deficiency, as part of hormonal replacement therapy in patients unable to tolerate oral progestins, or for the treatment of secondary amenorrhea.

Benefit Design:

Coverage for fertility drugs and vaginal progesterone is determined through prior authorization.

Prior Authorization Criteria

Fertility Agents:

- Coverage is provided for non-infertility indications and use for any male condition for 12 months.
- Coverage is provided for 12 months for female infertility treatment in the following situations:
 - Patient must be between 18 and 45 years of age.
 - Patient must not be using the fertility medication in conjunction with any type of Assisted Reproductive Technology (ART) procedure. ART procedures include In Vitro Fertilization (IVF), Gamete Intrafallopian Transfer (GIFT), Zygote Intrafallopian Transfer (ZIFT) and Intrauterine or Artificial Insemination.
 - Prescriber has performed an evaluation for other causes of infertility (e.g., prescriber has considered/ruled out hyperprolactinemia, thyroid dysfunction, premature or impending ovarian failure).
 - Prescriber has evaluated male partner for the presence of male factor infertility.

Vaginal Progesterone:

- Coverage is provided for progesterone supplementation in women with recurrent spontaneous abortion due to luteal phase deficiency, as part of hormonal replacement therapy in patients unable to tolerate oral progestins, or for the treatment of secondary amenorrhea.
- Coverage is approved for 3 months (secondary amenorrhea), 9 months (for women with recurrent

spontaneous abortion due to luteal phase deficiency), or 12 months (for progesterone supplementation as part of hormonal replacement therapy).

- Coverage is not provided in the presence of undiagnosed vaginal bleeding, liver dysfunction or liver disease, known or suspected malignancy of the breast and/ or genital organs, or a missed abortion.

References

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Product Information: Clomiphene citrate (*Clomid*[®] - Aventis) 1996

Product Information: Ganirelix (*Ganirelix Acetate*[®] - Organon) 2004

Product Information: Follitropin alpha (*Gonal-F*[®] - Serono) 2000

Product Information: Follitropin beta (*Follistim*[®] - Organon) 1998

Product Information: Gonadorelin (*Factrel*[®] - Wyeth Ayerst) 1997

Product Information: Lutropin alfa (*Luveris*[®] - Serono) 2004

Product Information: HCG (*A.P.L.*[®] - Wyeth Ayerst) 1998

Product Information: HCG (*Novare*[®] - Ferring) 1999

Product Information: HCG (*Pregnyl*[®] - Organon) 1998

Product Information: HCG (*Profasi HP*[®] - Serono) 1999

Product Information: Leuprolide (*Lupron*[®] - TAP) 2000

Product Information: Menotropins (*Humegon*[®] - Organon) 1998

Product Information: Menotropins (*Pergonal*[®] - Serono) 1994

Product Information: Menotropins (*Repronex*[®] - Ferring) 1999

Product Information: Nafarelin (*Synare*[®] - Searle) 1999

Product Information: Urofollitropin (*Bravelle*[™] - Ferring) 2002

Product Information: Urofollitropin (*Fertinex*[®] - Serono) 1999

Product Information: progesterone gel (*Crinone*[®] - Serono Laboratories, Inc.) 1998.

Product Information: progesterone gel (*Prochieve*[™] - Columbia Laboratories, Inc.) 2003.

Product Information: progesterone insert (Endometrin 8% - Ferring Laboratories, Inc.) 2008.

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