



Horizon BCBSNJ
Medical Necessity Guideline

Section
Policy Number
Effective Date
Review Date

Drugs
6/25/04
7/22/05, 3/28/08, 9/26/08,
5/12/09

Subject:

DRUG CLASS **Gonadotropin -Fertility Agent**

BRAND NAME **Pregnyl, Novarel**

(generic name) **(chorionic gonadotropin- hCG)**

IMPORTANT NOTE:

*The purpose of this policy is to provide general information applicable to the administration of outpatient prescription drug benefits that Horizon Blue Cross Blue Shield of New Jersey and Horizon Healthcare of New Jersey, Inc. (collectively "Horizon BCBSNJ") insures or administers. **Outpatient prescription drugs are not covered under all Horizon benefit plans.** If the member's contract benefits differ from the pharmacy guideline, the contract prevails. Although a service, supply drug or procedure may be medically necessary, it may be subject to limitations and/or exclusions under a member's benefit plan. If a service, supply drug or procedure is not covered and the member proceeds to obtain the service, supply drug or procedure, the member may be responsible for the cost. Decisions regarding treatment and treatment plans are the responsibility of the physician. This policy is not intended to direct the course of clinical care a physician provides to a member, and it does not replace a physician's or pharmacist's independent professional clinical judgment or duty to exercise special knowledge and skill in the treatment of Horizon BCBSNJ members. Horizon BCBSNJ is not responsible for, does not provide, and does not hold itself out as a provider of medical care. The physician remains responsible for the quality and type of health care services provided to a Horizon BCBSNJ member.*

Horizon BCBSNJ pharmacy guidelines do not constitute medical advice, authorization, certification, approval, explanation of benefits, offer of coverage, contract or guarantee of payment.

FDA-APPROVED INDICATIONS

- Prepubertal cryptorchidism not due to anatomic obstruction. In general, human chorionic gonadotropin (hCG) is thought to induce testicular descent in situations when descent would have occurred at puberty. HCG, thus may help to predict whether or not orchiopexy will be needed in the future. Although, in some cases, descent following hCG administration is permanent, in most cases the response is temporary. Therapy is usually instituted between the ages of 4 and 9.
- Selected cases of male hypogonadism secondary to pituitary failure (hypogonadotropic hypogonadism).
- Induction of ovulation and pregnancy in the anovulatory, infertile woman in whom the cause of anovulation is secondary and not due to primary ovarian failure, and who has been appropriately pretreated with human menopausal gonadotropins.

Human chorionic gonadotropin has not been demonstrated to be effective adjunctive therapy in the treatment of obesity. There is no substantial evidence that it increases weight loss beyond that resulting from caloric restriction, that it causes a more attractive or "normal" distribution of fat, or that it decreases the hunger and discomfort associated with calorie-restricted diets.

Medical Necessity Guideline:

1. The following questionnaire may be used to determine medical necessity of chorionic gonadotropin-HCG prescriptions.

CRITERIA FOR REVIEW

1. Does the patient have a diagnosis of infertility? [If the answer to this question is no, then skip to question 15.]	Yes	No
2. Is the patient male? [If the answer to this question is yes, may skip to question 12]	Yes	No
3. Will the patient be undergoing intrauterine insemination (IUI) [If the answer to this question is no, then skip to question 5.]		
4. Is the patient < 45 years of age? [If the answer is no, then please forward request to Horizon Pharmacy Service pharmacy_services@horizonblue.com . When Horizon approves please proceed to question 9.] [If the answer is yes, then skip to question 9].	Yes	No
5. Is or will the patient be undergoing follicle stimulation as part of an Assisted Reproductive Technology (ART) program (i.e., in vitro fertilization -IVF, gamete intrafallopian transfer -GIFT, tubal embryo transfer -TET, zygote intrafallopian transfer -ZIFT)? [If the answer is yes, then please forward request to Horizon Pharmacy Service pharmacy_services@horizonblue.com . When Horizon approves please proceed to question 9.]	Yes	No
6. Is or will the patient be undergoing treatment for induction of ovulation? [If the answer to this question is no, may skip to question 8]	Yes	No
7. Has or will the patient be pretreated with human menotropins? [Skip to question 9.]	Yes	No
8. Does the patient have a diagnosis of corpus luteum deficiency? [If the answer to this question is no, then no further questions required.]	Yes	No
9. Does the patient have a diagnosis of primary ovarian failure? [If the answer to this question is yes, then no further questions required.]	Yes	No
10. Has pregnancy been excluded as confirmed by a negative urine or serum pregnancy test? [If the answer to this question is no, then no further questions required.]	Yes	No
11. Will the patient require more than the dispensing limit of 2 vials every 30 days? [For patients undergoing ART or IUI procedures, no further questions.] [For all other indications, skip to question 14.]	Yes	No
12. Does the patient have a diagnosis of hypogonadotropic hypogonadism? [If the answer to this question is no, then no further questions required.]	Yes	No
13. Does the patient have prostatic carcinoma or other androgen dependent neoplasm? [If the answer to this question is yes, then no further questions required.]	Yes	No
14. Was the partner of the patient found to be fertile? [No further questions required.]	Yes	No
15. Does the patient have a diagnosis of prepubertal cryptorchidism not due to anatomical obstruction? [If the answer to this question is no, then no further questions required.]	Yes	No
16. Is the patient between the ages of 4 and 9 years?	Yes	No
17. Does the patient have a diagnosis of precocious puberty?	Yes	No

Guidelines for Approval

Duration of Approval - 3 months

Set 1 – Corpus luteum deficiency QL – 2 vials per 30 days		Set 2 – IUI - >= 45 years of age QL – 2 vials per 30 days NEED HORIZON APPROVAL	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	2	1	2
8	3	3	4
10	5	10	9
14	6		11
	9		
	11		
Set 3 – Induction of ovulation QL – 2 vials per 30 days		Set 4 – Prepubertal cryptorchidism QL – 9 vials per 30 days	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	2	15	1
6	3	16	17
7	5		
10	9		
14	11		
Set 5 – ART procedure – IVF,GIFT,TET,ZIFT QL – 2 vials per 30 days NEED HORIZON APPROVAL		Set 6 – IUI - < 45 years of age QL – 2 vials per 30 days	
Yes to question(s)	No to question(s)	Yes to question(s)	No to question(s)
1	2	1	2
5	3	3	9
10	9	4	11
	11	10	
Set 7 – Hypogonadotropic hypogonadism QL – 9 vials per 30 days			
Yes to question(s)		No to question(s)	
1		13	
2			
12			
14			

Horizon BCBSNJ Pharmacy Guideline Development Process: This Horizon BCBSNJ Pharmacy Guideline (the “Pharmacy Guideline”) has been developed by Horizon BCBSNJ’s Pharmacy Drug Policy Subcommittee, Clinical Issues Subcommittee, and Quality Improvement Committee which include practicing physicians and pharmacists. This guideline is consistent with generally accepted standards of medical and pharmacy practice, and reflects Horizon BCBSNJ’s view of the subject health care services, supplies drugs or procedures, and in what circumstances they are deemed to be medically necessary or experimental/ investigational in nature. This Pharmacy Guideline also considers whether and to what degree the subject health care services, supplies or procedures are clinically appropriate, in terms of type, frequency, extent, site and duration and if they are considered effective for the illnesses, injuries or diseases discussed. Where relevant, this Pharmacy Guideline considers whether the subject prescription drugs are being requested primarily for the convenience of the covered person or the health care provider. It may also consider whether the prescription drugs are more costly than alternative prescription drugs that are at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the relevant illness, injury or disease. In reaching its conclusion regarding what it considers to be the generally accepted standards of medical and pharmacy practice, Horizon BCBSNJ reviews and considers the following: all credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, physician and health care provider specialty society recommendations, the views of physicians and health care providers practicing in relevant clinical areas (including, but not limited to, the prevailing opinion within the appropriate specialty), the findings and directives of the Food and Drug Administration and any other relevant factor as determined by applicable State and Federal laws and regulations.

BLACK BOX WARNINGS

None

RATIONALE

The intent of the criteria is for patients to follow selection elements noted in labeling. Human chorionic gonadotropin (hCG) is indicated for prepubertal cryptorchidism not due to anatomic obstruction. Therapy is usually instituted between the ages of 4 and 9. HCG is also indicated in selected cases of hypogonadotropic hypogonadism (hypogonadism secondary to a pituitary deficiency) in males and the induction of ovulation and pregnancy in the anovulatory, infertile woman in whom the cause of anovulation is secondary and not due to primary ovarian failure, and who has been appropriately pretreated with human menopausal gonadotropins. Additional, compendial use includes human chorionic gonadotropin is indicated, in conjunction with menopausal gonadotropins or urofollitropin, to stimulate the development and maturation of multiple oocytes in ovulatory patients who are attempting to conceive by means of assisted reproductive technologies (ART), such as gamete intrafallopian transfer (GIFT) or *in vitro* fertilization (IVF). Because gonadotropins can harm a fetus, pregnancy must be ruled out before their use. Unless the patient is undergoing an Assisted Reproductive Technology (ART) procedure, the partner must have their fertility evaluated and be found fertile. Gonadotropins used for induction of ovulation should always be used in conjunction with some form of follicle stimulating hormone. HCG is contraindicated in patients with precocious puberty and prostatic carcinoma or other androgen dependent neoplasm.

Human chorionic gonadotropin will also be approved for treating infertility in women with corpus luteum insufficiency based on this as a compendial inclusion in the current MICROMEDEX.⁵

Horizon BCBSNJ has requested that all requests for patients undergoing an ART procedure – either a non-IUI procedure, or IUI and ≥ 45 years of age be sent to Horizon BCBSNJ services to verify whether the patient has coverage for this indication. If the patient qualifies for coverage, Horizon BCBSNJ will contact CVS Caremark to proceed with the clinical questions in the criteria. If the patient does not qualify for coverage, Horizon BCBSNJ will send a denial letter to the physician and inform CVS Caremark of this decision. Horizon BCBSNJ has requested a question addressing the dosage limit of 2 vials per 30 days for infertility indications.

ADDITIONAL INFORMATION

Dosage and Administration

For Intramuscular Injection Only:

The dosage regimen employed in any particular case will depend upon the indication for use, the age and weight of the patient, and the physician's preference. The following regimens have been advocated by various authorities:

Regimens for prepubertal cryptorchidism not due to anatomical obstruction:

Therapy is usually instituted between the ages of 4 and 9 years.

- 4000 USP units three times weekly for three weeks
- 5000 USP units every second day for four injections
- 15 injections of 500 to 1000 USP units over a period of 6 weeks
- 500 USP units three times weekly for four to six weeks. If this course of treatment is not successful, another is begun one month later, giving 1000 UPS units per injection.

Regimens for selected cases of male hypogonadotropic hypogonadism:

- 500 to 1000 USP units three times a week for three weeks, followed by the same dose twice a week for three weeks.
- 1000 to 2000 USP units three times weekly.
- 4000 USP units three times weekly for six to nine months, following which the dose may be reduced to 2000 USP units three times weekly for an additional three months.

Regimen for induction of ovulation and pregnancy in the anovulatory, infertile woman in whom the cause of anovulation is not due to primary ovarian failure and who has been appropriately pretreated with human menopausal gonadotropins:

- 5000 to 10,000 USP units one day following the last dose of menopausal gonadotropins. (note: 10,000 USP units is recommended in the labeling for menopausal gonadotropins)

Storage of products:

Pregnyl and Novarel may be stored at room temperature prior to reconstitution. After reconstitution, keep refrigerated and use within 60 days.

CONTRAINDICATIONS/WARNINGS/PRECAUTIONS

Contraindications:

- Precocious puberty
- Prostatic carcinoma or other androgen dependent neoplasia
- Prior allergic reaction to chorionic gonadotropin
- Pregnancy **Category X**- may cause fetal harm when administered to pregnant women

Warnings:

- Ovarian Hyperstimulation, a syndrome of sudden ovarian enlargement, ascities with or without pain, and/or pleural effusion.
- Enlargement of preexisting ovarian cysts or rupture of ovarian cysts with resultant hemoperitoneum
- Multiple births.
- Arterial thromboembolism.

Precautions:

- Since androgens may cause fluid retention, hCG should be used with caution in patients with cardiac or renal disease, epilepsy, migraine, or asthma.
- Induction of androgen secretion by hCG may induce precocious puberty in pediatric patients treated for cryptorchidism. Therapy should be discontinued if signs of precocious puberty occur.

REFERENCES

1. Pregnyl Product Information. Organon, Inc. August 1998.
2. Novarel Product Information. Ferring Pharmaceuticals. May 2001.
3. Facts and Comparisons. www.efactsweb.com. 2001.
4. American Hospital Formulary Service. American Society of Health-System Pharmacists. 2007.
5. MICROMEDEX Healthcare Series Online: Chorionic Gonadotropin. Thomson MICROMEDEX 2008.

Pharmacy Guidelines can be highly technical and are designed for use by the Horizon BCBSNJ professional staff in making coverage determinations. Members referring to this policy should discuss it with their treating physician or pharmacist, and should refer to their specific benefit plan for the terms, conditions, limitations and exclusions of their coverage.

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