



HEALTH NEW ENGLAND INFERTILITY PROTOCOL

Massachusetts and Connecticut mandate certain health insurance coverage of non-experimental infertility procedures recognized by the American Society for Reproductive Medicine (ASRM) or the American College of Obstetrics and Gynecology (ACOG). In accordance with these mandates, HNE will provide infertility benefits to medically infertile members with the goal of restoring normal reproductive capacity. Coverage for infertility services is available to members who meet the residency requirements, individual plan limitations, medical necessity and eligibility criteria outlined in this protocol. Residents of Connecticut must also meet the state defined age requirement.

I. DEFINITIONS

- A. **Infertility:** The condition of a Presumably Healthy individual who is unable to conceive or produce conception for a period of at least one year for under age 35, and for 6 months for ages over 35. Unable to conceive during these respective time periods means that you are of normal reproductive age, you would be expected to conceive absent a medical problem, and that you have been trying to conceive during these time periods. A female member must have 1 year of unprotected intercourse or physician supervised IUI for 12 cycles if under age 35, or 6 months of unprotected intercourse or physician supervised IUI for 6 cycles if age 35 or older. Absence of a male partner does not meet the definition of Infertility if there has been no attempt to conceive during the age respected time frames. IUI cycles for women who do not have exposure to sperm are at the members expense until the definition of infertility is met. Single or Same sex couples must self pay for 6-12 IUI cycles.(dependent on age) performed by a physician in the office with no resultant viable conception. Office and/or claim documentation may be requested.
- B. Criteria for meeting infertility – if a person conceives but is unable to carry pregnancy to live birth, the period of time attempting to conceive prior to achieving that pregnancy shall be included in the calculation of the 1 year or 6 month period.
- C. **Medically Necessary:** *For all ART (Assisted Reproductive Technology) infertility services [AI, IUI, FSH/IUI, IVF, ICSI] except donor egg (oocyte):* Infertility treatment is medically necessary when an individual (or couple) is medically infertile *and* such treatment is reasonably likely (at least a 5 % chance) to result in a viable offspring (take-home baby rate).
- D. **Presumably Healthy:** Presumably Healthy means presumably fertile (e.g. of normal reproductive age, not having undergone voluntary sterilization.)

II. COVERED INFERTILITY TREATMENTS

- A. **Initial Treatment Approaches:** HNE covers a variety of infertility treatments. Depending on the causes of infertility, however, some interventions may be less time consuming, less stressful, more cost effective and safer than others. These alternative approaches are generally recommended as first line and preferred courses of treatment, where appropriate. These treatments do not require prior authorization. If these

HNE INFERTILITY PROTOCOL - Continued

treatments do not result in a successful pregnancy, then treatment with one of the Assisted Reproductive Technologies may be indicated.

Examples of preferred courses of treatment include:

1. Surgical repair of fallopian tube(s)
2. Surgical and/or drug treatment for low sperm count and mobility
3. Ovulation Induction
4. Medical and surgical treatment of endometriosis

The infertility specialist is responsible for the initial assessment of whether infertility treatment is appropriate, and has the initial responsibility for ruling out medical conditions other than infertility that might be preventing or interfering with conception.

- B. Traditional Infertility Treatments:** HNE will cover traditional infertility treatments when Medically Necessary, including evaluation, infertility-related drugs, and Artificial Insemination/Intra-Uterine Insemination (AI/IUI) services. Cycles using IUI with or without ovulation induction, (Clomid or gonadotropin therapy) and all ART procedures require prior authorization.
- C. Assisted Reproductive Technology Procedures (IVF-ET, ICSI and donor oocyte):** HNE also covers the following non-experimental ART procedures, when Medically Necessary.
1. In Vitro Fertilization and Embryo-Transfer (IVF-ET)
 2. Sperm, egg, and/or inseminated egg procurement and processing, and banking of sperm and inseminated eggs, to the extent that such costs are not covered by the donor's insurer, if any, during an approved ART cycle. HNE does not cover any fees to a donor or program for donation of sperm/eggs, except in the case of severe male factor as described in the eligibility requirements.
 3. Intracytoplasmic Sperm Injection (ICSI) for the treatment of male factor infertility.
 4. Frozen Embryo Transfer

These procedures require prior approval from HNE. These procedures will only be covered where appropriate, subject to the medical circumstances of each case. In some cases, particular medical conditions indicate proceeding directly to one of these procedures, because the alternative courses of treatment listed in the preceding sections would not be appropriate. More specifically, the following medical conditions may suggest proceeding directly to IVF-ET, or ICSI:

1. Significant sperm abnormality.
2. Absent, blocked, or damaged fallopian tube(s) unresponsive or inappropriate for surgical repair or other treatments.
3. Stage IV endometriosis unresponsive or inappropriate for surgical repair or other treatments.

The authorization for ICSI has the same requirement as IVF-ET, with the exception that since ICSI is a male factor infertility issue, some of the preferred approaches listed above can be inapplicable.

HNE INFERTILITY PROTOCOL - Continued

III. RESIDENCY REQUIREMENTS AND INDIVIDUAL PLAN LIMITATIONS

- A. **Fully Funded health plan members:** HNE covers infertility services in accordance with the terms of this protocol for Massachusetts and Connecticut residents only. A Connecticut resident is covered for infertility benefits only until her 40th birthday as is specified by the Connecticut state infertility mandate. For members who reside in Connecticut and are age 40 years or older, infertility services are not covered. (Infertility services for Connecticut residents may end when the member turns 40 years old regardless of where the member is in the treatment cycle.)
- B. **State members (Group Insurance Commission [GIC] members):** HNE covers infertility services in accordance with the terms of this protocol regardless of whether the member resides in Massachusetts or Connecticut.
- C. **Self-Funded Group members:** Self-funded plans are not required to provide mandated infertility services. If a self-funded group offers infertility coverage, benefits will be provided to all members, regardless of their state of residency, as outlined in the group's Summary Plan Description, which may reference this protocol.

IV. ELIGIBILITY REQUIREMENTS

- A. Coverage for required infertility benefits will not be limited arbitrarily, but may be limited according to reasonable consideration of the individual member's medical history, hormone levels and age, medical necessity guidelines, provider standards and protocols, and legal requirements or limitations. Unless ineligible for reasons unrelated to this provision, and based upon the recommendation of the patient's clinician specialist, members who meet the following criteria (where relevant) are eligible for ART services.
- B. For a member to be considered for cycle initiation of a covered ART service:
 - 1. The member must meet the definition of medical infertility and infertility may not be the result of a previous sterilization or reversal thereof.
 - 2. For female members without a male partner, the provider must document at least 6-12 (dependent on age) cycles of intra-uterine inseminations performed by a physician in a medical office.
 - 3. Evaluation of Infertility – Requirements:
For a member to be considered for an ART procedure approval, and before cycle initiation, the member must have:
 - a. Semen analysis within one year or use of donor sperm from an accredited sperm bank
 - b. Uterine cavity evaluation within 2 years (sonohysterogram, hysterosalpingography, or hysteroscopy) If there has been a pregnancy and/or pregnancy loss since the last cavity evaluation, then a repeat evaluation is indicated before treatment resumes.
 - c. Laboratory studies
 - i. Normal Thyroid Stimulating Hormone (TSH) within one year
 - ii. Rubella immune
 - iii. Day 3 Follicle Stimulating Hormone (FSH) ≤ 13 , Estradiol (E2) ≤ 80 pg/ml, within 1 year if <40 years old; for women ≥ 40 years old, day 3 FSH and

HNE INFERTILITY PROTOCOL - Continued

- estradiol within 6 months and a Clomiphene Citrate Challenge Test (CCCT) d3 and d10 FSH \leq 13 within the year of the procedure requested.,
- d. Exceptions to a-c above
 - i. Day 3 labs and/or a CCCT will not be required if a gonadotropin cycle within 6 months documents an E2 > 500 with greater than 3 mature follicles and member is \leq 40 years old.
 - ii. An FET can be approved with only a normal uterine cavity evaluation
 4. Tobacco Use – due to the toxic effects of tobacco on female and male fertility and in pregnancy, both members of the couple must be non-smokers. If either member of the couple have smoked within the past 6 months:
 - a. A negative urine or serum cotinine level is required prior to approval of a cycle and as requested.
 - b. The provider must document that the member has stopped smoking
 5. BMI – Due to the association of obesity and infertility, the increased risks associated with infertility treatments in obese patients, and the increased risk to the mother, pregnancy, and baby associated with maternal obesity., the obese female patient must optimize her health status prior to receiving infertility therapy.
 - a. Patients with BMI >35 must submit documentation of a nutrition consult prior to an IUI or IVF cycle, and an Anesthesiology Consult prior to an IVF cycle.
 - b. In addition, patients with BMI >40 must submit the following documentation prior to approval of IVF and/or IUI
 - i. 6 months of active participation in a weight loss program
 - ii. Maternal Fetal Medicine Consult
 6. Additional Treatment Requirements before approval for an IVF cycle:
 - a. For women < 40 years of age, the member should complete at least 3 cycles of medicated IUI therapy. Medications may be Clomid or FSH with documented ovulation.
 - b. For women \geq 40 years of age, the member should complete at least 3 cycles of medicated IUI treatment. Medications may be Clomid or FSH with documented ovulation. At least one of the cycles must be with FSH.
 - c. Gonadotropin/IUI therapy will not be required if there is:
 - i. Bilateral Tubal obstruction
 - ii. Failure to conceive for 6 months after surgical treatment of tubal disease
 - iii. Severe male factor infertility documented on at least two separate semen analysis at least 2 weeks apart (< 10 million motile sperm on a routine semen analysis)
 7. Intra Cytoplasmic Sperm Injection (ICSI) will be recommended and approved for use within an IVF cycle if a severe male factor exists, including but not limited to the following:
 - a. Less than 10 million total motile sperm per ejaculate on two separate occasions at least 2 weeks apart (unprocessed semen analysis) or < 3 million total motile sperm on an IUI prepared specimen.
 - b. Poor (\leq 50 %) or failed fertilization in a previous IVF cycle
 8. Assisted Hatching is generally appropriate and will be approved in any of the following clinical situations:
 - a. Women > 38 years of age
 - b. Women with a history of 2 or more embryo transfers without a pregnancy

HNE INFERTILITY PROTOCOL - Continued

- c. Recommendation of the embryologist (e.g., in the presence of a thickened/hard zona).
9. Frozen Embryos Transfers will be approved with a normal uterine cavity evaluation within two years. Under the following conditions, cryopreserved embryos must be used prior to authorization for an additional fresh cycle:
 - a. For a woman < 35 years old with at least 3 embryos cryopreserved of the same developmental stage
 - b. For a woman \geq 35 with at least four embryos cryopreserved at the same developmental stage
10. Donor Sperm will be covered after preauthorization under the following conditions:
 - a. An HNE member has a partner diagnosed with severe male factor based on the results of 2 semen analyses.
 - b. The HNE member must not have any contraindications to pregnancy.
 - c. Three cycles may be authorized at a time.
 - d. Storage will be covered during active treatment cycles.
11. Donor Egg Therapy will be authorized for women who meet the definition of infertility and the member meets the criteria:
 - a. There is a diagnosis of premature ovarian failure or premature menopause. This diagnosis only applies to women under the age of 40, and must include one of the following:
 - i. The day 3 or day 10 FSH level is greater than 15. or
 - ii. There is an inadequate ovarian response during IVF attempts (<3 follicles >12 mm diameter) or;
 - iii. There is an inadequate ovarian response during FSH/IUI cycles
 - b. There is no medical history or physical condition which contradicts the therapy.
 - c. For women 40-42, there is normal ovarian reserves documented by a CCCT and complete but failed IVF attempts.
 - d. Anonymous donors must be \leq 35 years of age. Designated donor may be 35-39 years of age if there is a normal CCCT
 - e. Medications for the member-recipient will only be covered if the member has an HNE pharmacy benefit. Medication for the anonymous or designated donor in an approved cycle will not be covered.
12. Advanced Maternal Age will be considered the following way:
 - a. For women ages 40 to 42, an ART cycle will be approved one cycle at a time after meeting the above listed criteria including a normal CCCT, HSG, and at least one FSH/IUI cycle.
 - i. It is expected that an ART cycle will be cancelled if there are fewer than 3 follicles developed and/or the E2 level \leq 500 pg/ml.
 - ii. A repeat cycle may be approved after review of the prior cycles' outcome; at a minimum, it is expected that an ART cycle will have had more than 3 follicles developed and an estradiol level > 500 MIU/ml in order to offer a reasonable chance of success.
 - b. For women age 42, up to the member's 44th birthday, a single ART cycle may be approved for coverage using her own eggs based on her history and prior ART attempts including
 - i. Normal CCCT
 - ii. Development of 4 or more follicles and Estradiol > 500 m IU/ml following gonadotropin stimulation
 - iii. Prior ART cycle with transfer of at least 4 embryos of reasonable quality and

HNE INFERTILITY PROTOCOL - Continued

- iv. Fewer than 3 ART cycles prior to the woman's 42nd birthday
 - c. For women ages ≥ 44 : Fertility is not considered a natural state at or beyond age 44 regardless of hormonal testing, and all Assisted Reproductive Procedures are excluded at age 44 or greater.
 13. Infertility Services following Reversal of Sterilization: HNE will only cover infertility services after the reversal of a voluntary sterilization if:
 - a. In the case of female reversal of sterilization, there is documented tubal patency by hysterosalpingogram and there is failure to conceive after a period of 6 months to one year (age dependent), with unprotected intercourse or 6-12 (age dependent) cycles physician supervised exposures to donor sperm.
 - b. In the case of male reversal of sterilization, there is documentation of a normal semen analysis after the procedure and the couple are unable to conceive or produce conception after a period of one year from the date of the documentation of the successful reversal (ie, normal semen analysis);
 - c. All other conditions of this infertility protocol are met.
 14. All IUI, gonadotropin/IUI cycles must be prior authorized. No gonadotropin medications will be available without this authorization.
 15. Conversion from IUI treatment to IVF:
 - a. Patient must be ≤ 40 years old
 - b. There are 5 mature follicles.
 - c. Estradiol is ≥ 1000 pg/ml
 16. Approval for IVF/ICSI treatment may be up to three cycles at one time if the member is < 40 years old and in a fully-funded plan.. In general approval for ovulation induction/IUI cycles will include up to 4 cycles.
 17. (MESA) Microsurgical Epididymal Sperm Aspiration: HNE will cover male members with congenital absence or congenital obstruction of the vas deferens. (TESE) Testicular Sperm Extraction: HNE will cover male members with nonobstructive azoospermia.
- C. For IUI and/or IVF procedures, sperm used must be from the partner or tested and quarantined from an accredited sperm bank.

V. LIMITATIONS

In reviewing each request, HNE may consider the medical appropriateness of the services proposed. Such review will be based on the facts of the case in question, taking into consideration such factors as the following:

- Guidelines established by the American Society for Reproductive Medicine (ASRM) and American College of Obstetricians and Gynecologists (ACOG);
- Guidelines established by state regulatory agencies;
- Medical factors unique to the individual patient, such as: health history; medical condition, including any risk factors; and assessments of factors specific to infertility such as reproductive system condition and ovarian reserve;
- Weighing of health risks, if any, against chances for a successful pregnancy; and
- The professional opinion of the treating physician as to the advisability of the procedure.

VI. EXCLUSIONS

HNE does not cover the following:

- Reversal of male or female voluntary sterilization. (HNE will only cover infertility services after the reversal as outlined in Section IV.B.11.)
- Infertility treatment for Members who are not medically infertile.
- Any costs associated with any form of surrogacy, including gestational carriers.
- Non-mandated Infertility treatments.
- Cryopreservation of eggs.
- Procedures associated with gender selection, convenience, or genetic engineering.
- Early diagnosis of genetic or chromosomal abnormalities, including pre-implantation genetic diagnosis (PGD)
- Donation or sale of gametes or embryos.
- Clinical or laboratory research.
- Any fees to a donor or program for donation of sperm/eggs except as outlined in Section IV.B.8.
- Infertility medications for donors.
- Medications for ART cycles/attempts when the Member has not received HNE's Prior Approval for the ART cycle.
- Medications for gonadotropin/IUI cycles when the member has not received HNE's Prior Approval for the cycle.
- Frozen sperm or embryo storage fees not associated with an active cycle.
- ART for actively smoking members. Recent smokers must have documentation of a negative urine or serum cotinine level.

VII. PRIOR AUTHORIZATION AND APPROVAL

ART Infertility procedures, including IUI, gonadotropin/IUI cycles, require prior approval from HNE. Medications prescribed as a part of an ART cycle/attempt (including IVF, GIFT, ZIFT, ICSI, Donor Egg, and IUI) are covered for members with the pharmacy benefit when the cycle/attempt has been approved by HNE. If prior approval is not obtained for a cycle/attempt, related medications will not be covered. To ensure coverage, providers must request prior approval for these medications (see attachment: HNE Prior Approval Requirements for Infertility Medications and HNE Infertility Treatment Prior Approval Request Form for the specific medications and the process for obtaining prior approval). As described in the exclusion section of the protocol, infertility medications for donors are not covered. Therefore, even when donor egg cycles/attempts are approved, donor medications are not covered.

A request from the member's OB-GYN or other infertility specialist is required and must be forwarded to the HNE Health Services Management Department for approval for each cycle before arrangements for initiation of the cycle are made. HNE may review the medical record and other related records to assure that all eligibility and medical conditions have been met. HNE will notify the member and provider in writing when the service for that cycle is authorized. For members < 40 years old, up to 3 cycles may be approved on the prior authorization form.

ART procedures must be performed by an HNE provider at a contracting facility in order for it to be covered as outlined in the HMO and GIC contracts. Self-funded members must go to a contracting facility for authorization and coverage of in-network benefits. All members should refer to their explanation of coverage policy for limitation/exclusions to this protocol.

VIII. REFERENCES

- Aboulghar, M., MD, Mansour, R., MD, Serour, G., MD, Adrazek, A., MD, Amin, Y., MD, and Rhodes, C., MRCOG, "Controlled ovarian hyperstimulation and intrauterine insemination for treatment of unexplained infertility should be limited to a maximum of three trials," *Fertility and Sterility*, Vol. 75, No. 1, January 2001, p. 88-91.
- American Society for Reproductive Medicine, "Optimal Evaluation of the Infertile Female," A Practice Committee Report: A Committee Opinion, June 2000, p. 1-6.
- American Society for Reproductive Medicine, "Aging and Infertility in Women," A Practice Committee Report: A Committee Opinion, January 2002, p. 1-6.
- Dunoso P, Staessan C, Fauser BC, Devroey P, Current Value of Preimplantation genetic aneuploidy screening in IVF, *Hum Reprod update* 2007 (Jan-Feb) 13(1):15-25.
- Jones, H., Jr., MD, and Toner, J., MD, PhD, "The Infertile Couple," *The New England Journal of Medicine*, December 2, 1993, p. 1710-1713.
- Kuliev A, Verlinsky Y. The role of preimplantation genetic diagnosis in women of advanced reproductive age. *Curr Opin Obstet Gynecol* 2003; 15(3):233-8.
- Massachusetts Division of Insurance (DOI) Regulation 211 CMR 37.00 - Infertility Benefits
- Magarelli PC, Pearlstone AC, Buyalos RP. Discrimination between chronological and ovarian age in infertile women aged 35 years and older: predicting pregnancy using basal FSH, age and number of OI/UI cycles. *Hum Reprod*, 1996 Jun, 11:6, 1214-9.
- Palermo, G., MD, Cohen, J., MD, and Rosenwaks, Z., MD, "Intracytoplasmic sperm injection: a powerful tool to overcome fertilization failure," *Fertility and Sterility*, Vol. 65, No. 5, May 1996, p. 899-908.
- Philips, Z., Barraza-Llorens, M., and Posnett, J., "Evaluation of the relative cost-effectiveness of treatments for infertility in the UK," *Human Reproduction*, Vol. 15, No. 1, 2000, pp. 95-106.
- Ramlau-Hansen CH, Thulstrup AM, Nohr EA, et al, Subfecundity in overweight and obese couples, *Hum Reprod* 2007 (Jun); 22(6):1634-7.
- Reindollar RH, Regan MM, Neumann PJ, Levine B, Thornton K, Alper M, Goldman M, A Randomized Clinical Trial to Evaluate Optimal Treatment for unexplained Infertility: the Fast Track and Standard Treatment (FASTT) Trial, *Fertility and Sterility*, Vol 94, no. 3 August 2010, p.888-898.
- Seif, M M W, Edi-Osagie, E C O, Farquhar, C, Hooper, L, Blake, D, McGinlay, P. Assisted hatching on assisted conception (IVF & ICSI).[update in Cochrane Database Syst Rev. 2006;(1).
- Sharma, V., PhD, FRCOG, Allgar, V, PhD, and Rajkhowa, M. MD, MRCOG, "Factors influencing the cumulative conception rate and discontinuation of in vitro fertilization treatment for infertility," *Fertility and Sterility*, Vol. 78, No. 1, July 2002, p. 40-46.
- Sills ES, Palermo GD. Preimplantation genetic diagnosis for selective sex selection, the IVF market economy, and the child – another long day's journey into night? *J Assist Reprod Genet* 2002; 19(9):431-2.
- Society for Assisted Reproductive Technology and the American Society for Reproductive Medicine, "Assisted reproductive technology in the United States: 1999 results generated from the American Society for Reproductive Medicine/ Society for Assisted Reproductive Technology Registry," *Fertility and Sterility*, Vol. 78, No. 5, November 2002, p. 918-931.
- Voorhis, B., MD, Barnett, M., RPh, MSc, Sparks, A., PhD, Syrop, C., MD, Rosenthal, G., MD, and Dawson, J., ScD, "Effect of the total motile sperm count on the efficiency and cost-effectiveness of intrauterine insemination and in vitro fertilization," *Fertility and Sterility*, Vol. 75, No. 4, April 2001, p. 661-668.