Clinical Policy: Fertility Preservation

Reference Number: PA.CP.MP.130 Coding Implications
Effective Date: 11/18
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Description
Male and female fertility may be transiently or permanently affected by medical treatments such as gonadotoxic therapy, cytotoxic chemotherapy, or radiation therapy, as well as by other iatrogenic causes. Rates of permanent infertility and compromised fertility after medical treatment vary and depend on many factors, including the drug, size and location of the radiation field if applicable, dose, dose-intensity, method of administration (oral versus intravenous), disease, age, treatment type and dosages, and pretreatment fertility.

Policy/Criteria

I. It is the policy of Pennsylvania Health and Wellness® (PHW) that, when a covered benefit under the member's benefit plan contract, any of the following procedures are **medically necessary** for women and adolescent girls prior to commencing treatment that is likely to cause infertility (excluding voluntary sterilization):
   A. Embryo cryopreservation;
   B. Cryopreservation of mature oocytes;
   C. Ovarian transposition (oophoropexy);
   D. Radiation (gonadal) shielding;
   E. Conservative gynecologic surgery including but not limited to the following:
      1. Radical trachelectomy in early stage cervical cancer (i.e., stage IA2 to IB cervical cancer with diameter <2 cm and invasion <10 mm);
      2. Ovarian cystectomy for early-stage ovarian cancer.

II. It is the policy of PHW that, when a covered benefit under the member's benefit plan contract, the following procedures are **medically necessary** for men and adolescent boys prior to commencing treatment that is likely to cause infertility (excluding voluntary sterilization):
   A. Cryopreservation of sperm;
   B. Radiation (gonadal) shielding.

III. It is the policy of PHW that the following procedures for women and adolescent girls prior to commencing treatment that is likely to affect fertility are considered **investigational**:
   A. Cryopreservation of immature oocytes;
   B. Ovarian tissue cryopreservation and transplantation procedures;
   C. Ovarian suppression with gonadotropin releasing hormone (GnRHa) or antagonists.

IV. It is the policy of PHW that the following procedures for men and adolescent boys prior to commencing treatment that is likely to affect fertility are considered **investigational**:
   A. Testicular suppression with GnRHa or antagonists;
   B. Testicular tissue or spermatogonial cryopreservation;
   C. Reimplantation or grafting of human testicular tissue.

Background
The most frequent cause of impaired fertility in male cancer survivors is chemotherapy or radiation-induced damage to sperm. The fertility of female survivors may be impaired by any treatment that damages immature eggs, affects the body's hormonal balance, or injures the reproductive organs. Fertility preservation is an essential part of the management of adolescents and young adults who are at risk for infertility due to cancer treatments, or bilateral ovary or testicular removal for treatment of disease.

Embryo cryopreservation is an established fertility preservation method, and it has routinely been used for storing surplus embryos after in vitro fertilization. Cryopreservation of unfertilized oocytes is an option, particularly for patients who do not have a male partner, do not wish to use donor sperm, or have religious or ethical objections to embryo freezing. Success rates for this procedure have improved significantly, with some reproductive specialty centers reporting success rates comparable to those obtained using unfrozen eggs, especially in younger women. Like embryo cryopreservation, this technique also requires ovarian stimulation and ultrasound-guided oocyte retrieval.

The effectiveness of ovarian suppression with GnRHa or antagonists is inconclusive. There is conflicting evidence to recommend GnRHa as a method of fertility preservation. Studies to date have not provided definitive data demonstrating that GnRHa preserves fertility, and it remains the subject of ongoing research.

American Society of Clinical Oncology (ASCO)
ASCO's recommends discussing fertility preservation with all patients of reproductive age (and with parents or guardians of children and adolescents) if infertility is a potential risk of therapy, as early as possible, before treatment starts.

For males who express an interest in fertility preservation, sperm cryopreservation is the only established fertility preservation method. ASCO notes that hormonal therapy in men has not shown to be successful in preserving fertility. Per ASCO, other methods, including testicular tissue cryopreservation for the purpose of future reimplantation or grafting of human testicular tissue are experimental.

For females who express an interest in fertility preservation, both embryo and oocyte cryopreservation are established fertility preservation methods. Other options for women include ovarian transposition (oophoroexy) when pelvic radiation therapy for cancer treatment is performed or conservative gynecological surgery and radiation options. ASCO notes that ovarian tissue cryopreservation for the purpose of future transplantation is experimental. They note also, there is insufficient evidence regarding the effectiveness of ovarian suppression (gonadotropin-releasing hormone analogs) to preserve fertility.

The ASCO guidelines continue to note that there is conflicting evidence to recommend GnRHa and other means of ovarian suppression for fertility preservation. However, the Panel recognizes that, when proven fertility preservation methods are not feasible, and in the setting of young women with breast cancer, GnRHa may be offered to patients in the hope of reducing the likelihood of chemotherapy-induced ovarian insufficiency. GnRHa should not be used in place

of proven fertility preservation methods. The panel notes that the field of ovarian tissue cryopreservation is advancing quickly and may evolve to become standard therapy in the future, although at the time of publication, it remains experimental.[10]

For children, ASCO recommends using established methods of fertility preservation (semen cryopreservation and oocyte cryopreservation) for postpubertal minor children, with patient assent, if appropriate, and parent or guardian consent.[1] For prepubertal children, the only fertility preservation options are ovarian and testicular cryopreservation, which are investigational.[10]

National Comprehensive Care Network (NCCN)
NCCN guidelines on Adolescent and Young Adult Oncology note that mature oocyte cryopreservation is no longer considered investigational, however, embryo cryopreservation is preferred if there is an identified sperm donor.[2]

Ovarian tissue cryopreservation is a promising, but less well-studied strategy for female fertility preservation when there is insufficient time for oocyte or embryo cryopreservation and/or the patient is prepubertal. While tissue cryopreservation is still considered investigational at some institutions, it may be discussed as an option for fertility preservation.[2]

Some data suggest that menstrual suppression with GnRHa may protect ovarian function. However, evidence that menstrual suppression with GnRHa protect ovarian function is insufficient, so this procedure is not currently recommended as an option for fertility preservation.[2]

American College of Obstetricians and Gynecologists (ACOG)
For young women who have completed sexual development, GnRHa, such as leuprolide acetate, have been used to induce ovarian quiescence to preserve ovarian function and fertility after cytotoxic treatment. Leuprolide acetate is not recommended for prepubertal girls. There still is no conclusive evidence that demonstrates efficacy of GnRHa, and studies are primarily observational regarding their effectiveness in fertility preservation. The use of GnRHa should be considered and discussed with premenopausal patients who will be treated with chemotherapeutic agents. Because GnRHa have mixed results in fertility preservation with trends toward more favorable outcomes, GnRHa therapy may be recommended as an adjuvant to chemotherapy. A meta-analysis of females 14–45 years of age demonstrated that co-treatment with GnRH agonists during chemotherapy was associated with increased odds of maintaining ovarian function and achieving pregnancy after treatment.[11]

Coding Implications
This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage.

Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT® Codes	Description
00840	Anesthesia for intraperitoneal procedures in lower abdomen including laparoscopy; not otherwise specified
57531	Radical trachelectomy, with bilateral total pelvic lymphadenectomy and para-aortic lymph node sampling biopsy, with or without removal of tube(s), with or without removal of ovary(s)
58825	Transposition, ovary(s)
58970	Follicle Puncture for oocyte retrieval, any method
76856	Ultrasound, pelvic (nonobstetric), real time with image documentation; complete
76948	Ultrasonic guidance for aspiration of ova, imaging supervision and interpretation
77334	Treatment devices, design and construction, complex (irregular blocks, special shields, compensators, wedges, molds or casts)
82670	Estradiol
83001	Gonadotropin; follicle stimulating hormone (FSH)
83002	Gonadotropin; luteinizing hormone (LH)
84144	Progesterone
84702	Gonadotropin; chorionic (hCG); quantitative
89250	Culture of oocyte(s)/embryo(s), less than 4 days
89251	Culture of oocyte(s)/embryo(s), less than 4 days; with co-culture of oocyte(s)/embryos
89254	Oocyte identification from follicular fluid
89258	Cryopreservation, embryo(s) (freezing services, not storage)
89259	Cryopreservation; sperm
89268	Insemination of oocytes
89272	Extended culture of oocytes/embryo(s), 4-7 days
89280	Assisted oocyte fertilization, microtechnique; less than or equal to 10 oocytes
89281	Assisted oocyte fertilization, microtechnique; greater than 10 oocytes
89320	Semen analysis; volume, count motility and differential
89337	Cryopreservation, mature oocyte(s)
89352	Thawing of cryopreserved; embryo(s)
89353	Thawing of cryopreserved; sperm/semen, each aliquot
99000	Handling and/or conveyance of specimen for transfer from office to a laboratory
99001	Handling and/or conveyance of specimen for transfer from the patient in other than an office to a laboratory (distance may be indicated)
99070	Supplies and materials (except spectacles), provided by the physician or other qualified health care professional over and above those usually included with the office visit or other services rendered (list drugs, trays, supplies, or materials provided)
99078	Physician or other qualified health care professional qualified by education, training, licensure/regulation (when applicable) educational services in a group setting (eg, prenatal, obesity, or diabetic instructions)
99199	Unlisted special service, procedure or report

HCPCS Codes	Description
S4030	Sperm procurement and cryopreservation services; initial visit
S4031	Sperm procurement and cryopreservation services; subsequent visit

CPT Codes Considered Investigational

CPT® Codes	Description
0357T	Cryopreservation; immature oocyte(s)
89335	Cryopreservation, reproductive tissue, testicular
0058T	Cryopreservation; reproductive tissue, ovarian

ICD-10-CM Diagnosis Codes that Support Coverage Criteria

ICD-10-CM Code	Description
C00.0-D49	Neoplasms
D27.0	Benign neoplasm of right ovary
D27.1	Benign neoplasm of left ovary
D39.10-D39.12	Neoplasm of uncertain behavior of ovary
D40.10-D40.12	Neoplasm of uncertain behavior of testis
N70.01- N70.03	Acute salpingitis and oophorits
N70.11- N70.13	Chronic salpingitis and oophoritis
N83.511-N83.519	Torsion of ovary and ovarian pedicle
Z31.84	Encounter for fertility preservation procedure

Reviews, Revisions, and Approvals	Date	Approval Date
Policy developed.	10/18	

References

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12. Sonmezer M, Oktay K. Fertility preservation in patients undergoing gonadotoxic treatment or gonadal resection. In: UpToDate, Barbieri RL (Ed), UpToDate, Accessed September 7, 2018.