

# Clinical Policy: Fertility Preservation

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## Description

Fertility may be transiently or permanently affected by medical treatments such as bilateral oophorectomy, 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.

*Note: For criteria related to cryopreservation, please see CP.MP.55 Assisted Reproductive Technologies.*

## Policy/Criteria

- I. It is the policy of health plans affiliated with Centene Corporation® that, when a covered benefit under the member's/enrollee's benefit plan contract, any of the following procedures are **medically necessary** for adults and adolescents with a female reproductive system prior to commencing medically necessary treatment that is likely to cause infertility (excluding voluntary sterilization):
  - A. Ovarian stimulation and retrieval of oocytes;
  - B. Ovarian tissue retrieval and all of the following:
    1. Ovarian tissue is free from malignancy;
    2. Insufficient time for oocyte retrieval or member/enrollee is prepubertal;
  - C. Ovarian transposition (oophoropexy).

*Note: For those with female reproductive systems  $\geq$  age 40 requesting retrieval of their own oocytes, documentation is required noting that the treating provider has evaluated age, infertility risk factors, measure of ovarian reserve, and considers use of the member/enrollee's own oocytes a viable strategy for attempting future conception.*

- II. It is the policy of health plans affiliated with Centene Corporation that there is insufficient evidence in the published peer-reviewed literature to support the use of the following procedures for fertility preservation in adults and adolescents with a female reproductive system prior to commencing treatment that is likely to affect fertility:
  - A. Ovarian suppression with gonadotropin releasing hormone (GnRH) agonist or antagonists.
- III. It is the policy of health plans affiliated with Centene Corporation that, when a covered benefit under the member's/enrollee's benefit plan contract, the following procedures are **medically necessary** for adults and adolescents with a male reproductive system prior to

commencing medically necessary treatment that is likely to cause infertility (excluding voluntary sterilization):

A. Sperm extraction and retrieval procedures.

**IV.** It is the policy of health plans affiliated with Centene Corporation that there is insufficient evidence in the published peer-reviewed literature to support the use of the following procedures for fertility preservation in adults and adolescents with a male reproductive system prior to commencing treatment that is likely to affect fertility:

A. Testicular suppression with GnRH agonist or antagonists;

B. Reimplantation or grafting of human testicular tissue.

### **Background**

An estimated 4.4% of all new cancer cases occur among adolescents and young adults between the ages of 15 to 39. Cancer patients are surviving at increasing rates, but successful treatment in younger patients can often be gonadotoxic and lead to late and long-term effects such as infertility. Treatment can affect fertility by causing damage to immature eggs and reproductive organs and affecting the body's hormones. Fertility preservation is an essential part of the management of adolescents and young adults who are at risk for infertility due to cancer treatments.<sup>11</sup>

Gonadotoxic treatments include chemotherapy, radiation, and surgical resection (for treatment of disease or gender affirmation surgery). Additionally, chemotherapy can be used for noncancerous conditions such as autoimmune diseases, like systemic lupus erythematosus (SLE), and hematological disease. Prompt counseling regarding available options for fertility preservation for iatrogenic infertility should be provided to patients prior to undergoing any gonadotoxic treatments.<sup>10</sup>

*American Society for Reproductive Medicine (ASRM)*<sup>10\*</sup>

The 2019 ASRM committee opinion for Fertility Preservation in Patients Undergoing Gonadotoxic Therapy or Gonadectomy affirmed that ovarian tissue cryopreservation is no longer considered experimental for prepubertal girls and for those who cannot delay cancer treatment to undergo ovarian stimulation and oocyte retrieval. The committee states, “data on the efficacy, safety, and reproductive outcomes after ovarian tissue cryopreservation are still limited. Given the current body of literature, ovarian tissue cryopreservation should be considered an established medical procedure with limited effectiveness that should be offered to carefully selected patients.”

The guideline states that the use of gonadotropin releasing hormone (GnRH) analogs for ovarian protection during chemotherapy remains controversial: “further studies are required to establish the efficacy of this treatment and to determine which patients are the best candidates for its use.” Furthermore, GnRH analog therapy for fertility preservation in males has failed to demonstrate effectiveness.

*American Society of Clinical Oncology (ASCO)<sup>5\*</sup>*

The ASCO 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 those with a male reproductive system who express an interest in fertility preservation, sperm cryopreservation is the only established fertility preservation method. ASCO notes that in these patients, hormonal therapy 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 those with a female reproductive system who express an interest in fertility preservation, both embryo and oocyte cryopreservation are established fertility preservation methods. The ASCO notes that evidence for ovarian tissue cryopreservation for the purpose of future transplantation remains insufficient, however, the field of ovarian tissue cryopreservation is advancing quickly and may evolve to become standard therapy in the future though it should also be noted that further investigation is needed to confirm whether it is safe in patients with leukemias. They note also, there is insufficient evidence regarding the effectiveness of ovarian suppression with GnRH agonist or antagonists to preserve fertility.

*National Comprehensive Cancer Network (NCCN)<sup>8\*</sup>*

NCCN guidelines on Adolescent and Young Adult Oncology note that oocyte or embryo cryopreservation is recommended for those that can delay cancer therapy for approximately three weeks. Ovarian tissue cryopreservation is a promising strategy for fertility preservation when there is insufficient time for oocyte or embryo cryopreservation and/or the patient is prepubertal. Hormonal stimulation is not required with this technique, therefore there is no delay in the initiation of treatment. This procedure is not appropriate for certain patients, including carriers of BRCA mutations due to the increased risk of ovarian cancer and those with cancer if potential exists for reintroduction of malignant cells with grafting. While ovarian tissue cryopreservation is still considered investigational at some institutions, it may be discussed as an option for fertility preservation.

Some data suggests menstrual suppression with GnRH agonists may protect ovarian function. However, evidence that menstrual suppression with GnRH agonists provides adequate protection of the ovaries is controversial, so this procedure is not currently considered a form of fertility preservation.

*American College of Obstetricians and Gynecologists (ACOG)<sup>6\*</sup>*

ACOG's Gynecologic Issues in Children and Adolescent Cancer Patients and Survivors committee opinion states that "cryopreservation of oocytes or embryos may be offered before cancer treatments if there is adequate time and a safe method for ovarian stimulation. Ovarian tissue extraction and cryopreservation have been shown to have some success with posttreatment auto transplantation after chemotherapy."

For young individuals with a female reproductive system who have completed sexual development, GnRH agonists and antagonists 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 prior to puberty. There still is no conclusive evidence that demonstrates efficacy of GnRH agonists and antagonists, and studies are primarily observational regarding their effectiveness in fertility preservation.

*\*Note: For criteria related to cryopreservation, please see CP.MP.55 Assisted Reproductive Technologies.*

### Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2024, American Medical Association. All rights reserved. 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
00922	Anesthesia for procedures on male genitalia (including open urethral procedures); seminal vesicles
53899	Unlisted procedure, urinary system
55870	Electroejaculation
55899	Unlisted procedure, male genital system
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
82670	Estradiol; total
83001	Gonadotropin; follicle stimulating hormone (FSH)
83002	Gonadotropin; luteinizing hormone (LH)
84144	Progesterone
84702	Gonadotropin; chorionic (hCG); quantitative
89254	Oocyte identification from follicular fluid
89320	Semen analysis; volume, count motility and differential
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)

CPT® Codes	Description
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
S4028	Microsurgical epididymal sperm aspiration (MESA)

**CPT Codes that do not support medical necessity**

CPT® Codes	Description
53899	Unlisted procedure, urinary system
55899	Unlisted procedure, male genital system
89398	Unlisted reproductive medicine laboratory procedure

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy adopted from Health Net NMP512, Fertility Preservation in Cancer Patients. Expanded criteria to include iatrogenic causes of infertility. Added the following ICD-10 codes: D27.0, D27.1, N70.03, N70.13, N83.51.	9/16	10/16
Removed CPT 0375T – code deleted 1/1/20	04/20	
References reviewed and updated. Replaced ‘members’ with ‘members/enrollees’ in all instances. Specialty review completed.	09/20	09/20
Revised description of CPT-82670. CPT-0058T deleted in 2021. “Experimental/investigational” verbiage replaced with descriptive language in policy statement III and IV.	02/21	
Annual review. References reviewed and updated. Changed “review date” in the header to “date of last revision” and “date” in the revision log header to “revision date.”	09/21	09/21
Annual review. Replaced all instances of female and male with descriptive, gender-neutral verbiage. Added code 89398 to table of CPT codes considered investigational. References reviewed and updated.	05/22	05/22
In description, removed “male and female” from introductory sentence about medical causes of impaired fertility.	09/22	
Annual review. Specified in sections I. and III. that the treatment causing risk to fertility was medically necessary. Removed "embryo cryopreservation", "cryopreservation of mature oocytes", "conservative gynecologic surgery (radical trachelectomy and ovarian cystectomy)" and "radiation (gonadal) shielding" from section I. Added "ovarian stimulation and retrieval of oocytes" and "ovarian tissue retrieval" to section I. Included "Note: For those with female reproductive systems > age 40..." to criteria and background sections. Removed	05/23	05/23

Reviews, Revisions, and Approvals	Revision Date	Approval Date
"cryopreservation of immature oocytes" and ovarian tissue cryopreservation and transplantation procedures" from section II. Added "sperm extraction procedures and retrieval procedures" to section III and removed "cryopreservation of sperm" and radiation (gonadal) shielding". Removed "testicular tissue or spermatogonial cryopreservation" from section IV. Criteria section reformatted for organizational purposes. Background updated. Added CPT codes 00922, 53899, 55899, and 55870. Removed CPT codes 57531, 77334, 89250, 89251, 89258, 89259, 89268, 89272, 89280, 89281, 89337, 89352, 89353. Added HCPCS codes S4028 and removed HCPCS codes S4030 and S4031. Added CPT code 53899 and 55899 and removed 89335 from the "does not support" table. References reviewed and updated. Internal specialist review.		
Annual review. Minor rewording under description and background with no impact to criteria. References reviewed and updated. Reviewed by internal specialist.	01/24	01/24
Annual review. References reviewed and updated. Reviewed by external specialist.	01/25	01/25

## References

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### **Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note: For Medicaid members/enrollees**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note: For Medicare members/enrollees**, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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