Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Joint Medical Policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and is therefore subject to change.

***Current Policy Effective Date: 9/1/24**
(See policy history boxes for previous effective dates)

Title: Infertility Related to Cancer Treatment

Description/Background

American Society for Reproductive Medicine (ASRM) Practice Committee (2023)[1] issued a new definition of "infertility" as follows:

"Infertility" is a disease, condition, or status characterized by any of the following:

- The inability to achieve a successful pregnancy based on a patient's medical, sexual, and reproductive history, age, physical findings, diagnostic testing, or any combination of those factors.
- The need for medical intervention, including, but not limited to, the use of donor gametes or donor embryos in order to achieve a successful pregnancy either as an individual or with a partner.
- In patients having regular, unprotected intercourse and without any known etiology for either partner suggestive of impaired reproductive ability, evaluation should be initiated at 12 months when the female partner is under 35 years of age and at six months when the female partner is 35 years of age or older.

The diagnosis and treatment of cancer may pose a threat to fertility. Given the reproductive risks of many cancer therapies in those of reproductive age, and improved long-term survival, there is interest in preserving the reproductive options for cancer patients. It is recommended that patients who are diagnosed with cancer and are preparing to undergo gonadotoxic medical therapy or radiation therapy, or gonadectomy, should be provided with counseling regarding available options for fertility preservation.[2]

As of March 2024, 15 states have laws requiring insurers to cover fertility preservation procedures for cancer patients and others who are facing potential infertility as a result of medical treatment. Where legislation exists, the state determines the definition of infertility and what services are covered; these mandates supersede this policy.[3]

Gender Descriptions
The term *biological female* used in this policy refers to members with two X chromosomes (or no Y chromosome) and includes members with gender identities other than female.

The term *biological male* used in this policy refers to members with XY chromosomes and includes members with gender identities other than male.

The terms *biological female* and *biological male* are used to clarify the reproductive capacity of the member and are not meant to exclude members with other gender identities/expressions.

Regulatory Status

NA

Medical Policy Statement

Preservation of fertility (including collection of oocytes and spermatozoa; cryopreservation, storage and thawing of embryos, oocytes and spermatozoa) may be considered established for individuals diagnosed with cancer and at risk for treatment-related infertility, when criteria are met.

Inclusionary and Exclusionary Guidelines

Benefit Information
- The member must have coverage on the date that services are performed.
- Benefit documents may exclude cryopreservation, storage or thawing of embryos, oocytes or spermatozoa.
- Benefit documents may allow fertility preservation for indications other than cancer treatment; indications other than cancer treatment are not discussed in this policy.
- For medications that may be used during the fertility preservation process, the individual's prescription drug benefit should be referenced.

State Legislation
States may have mandates that define when fertility preservation services are covered, and what specific services are covered. These mandates supersede this medical policy.

Inclusions:
- Preservation of fertility in a post-pubertal biological female or a post-pubertal biological male may be considered established when:
    - The individual is diagnosed with cancer, and the cancer treatment will result in irreversible infertility, such as with:
        - Gonadotoxic chemotherapy
        - Radiation therapy of the pelvis, lower abdomen or total body
        - Surgical removal of ovaries or testicles (testes)

Procedures that may be considered established in fertility preservation:

- Collection of mature oocytes and spermatozoa
- Cryopreservation of embryos, mature oocytes and spermatozoa
- Storage of embryos, mature oocytes and spermatozoa for up to two years
- Thawing of embryos, mature oocytes and spermatozoa within two years of the procurement
- Culture of oocytes
- Ovarian transposition (in anticipation of pelvic or lower abdominal radiation)
- Embryo transfer, back to the member, within two years from cryopreservation

Exclusions:

- Storage of sperm, oocytes or embryos for longer than two years
- Co-culture of embryo(s)
- Post-menopausal females
- Individuals who have undergone elective sterilization (vasectomy, tubal sterilization), with or without reversal
- Request for fertility preservation that does not meet inclusion criteria
- Other assisted reproductive techniques, unless the member has additional benefit coverage for these services.
- Cryopreservation of ovarian tissue, immature oocytes, and testicular tissue in post-pubertal biological males.
- Cryopreservation of testicular tissue in pre-pubertal biologic males.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

58679[a]	58825	58970	58974	76948
89250	89254	89258	89259	89268
89337	89342	89343	89346	89352
89353	89356			

Other codes (investigational, not medically necessary, etc.):

89335	89344	89354	89398[b]

a When the code represents laparoscopy for transposition of ovaries
b When this code represents cryopreservation of ovarian tissue or immature oocytes.

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

Improvements in treating cancer have enabled many younger persons with cancer to survive. Five-year survival rates with testicular cancer, hematologic malignancies, breast cancer, and other cancers that strike young people may be 90% or greater. However, treatment of these cancers is often detrimental to both male and female reproductive function.[5]

The testis is highly susceptible to the toxic effects of radiation and chemotherapy at all stages of life. Cytotoxic chemotherapy and radiotherapy may produce long-lasting or persistent damage to primordial sperm cells, leading to oligo- or azoospermia. The most common strategy to preserve fertility is cryopreservation of sperm before treatment for later use. Cryopreservation of testicular tissue from prepubescent males remains experimental.[5]

Female fertility also may be impaired following surgery, chemotherapy, or radiotherapy treatment for cancer. Ovarian damage is drug- and dose-dependent and is related to age at the time of treatment, with progressively smaller doses producing ovarian failure as the patient's age increases. Total body, abdominal, or pelvic irradiation may cause ovarian and uterine damage, depending on radiation dose, fractionation schedule, and age at the time of treatment. In females, the clinical situation dictates the strategy that is used for fertility preservation, and may include oocyte or embryo cryopreservation or ovarian transposition.

As part of education and informed consent before cancer therapy, health care providers (including medical oncologists, radiation oncologists, gynecologic oncologists, urologists, hematologists, and surgeons) should address the possibility of infertility with patients treated during their reproductive years.[4]

Cryopreservation of Ovarian Tissue

Clinical Context and Therapy Purpose

The purpose of cryopreservation of ovarian tissue in individuals with cancer who will undergo treatment that could precipitate infertility is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with cancer who undergo treatment that could precipitate infertility.

Interventions

The therapy being considered is cryopreservation of ovarian tissue.

Comparators

The following practice is currently being used to make decisions about infertility: cryopreservation of embryos but not of ovarian tissue.

Outcomes

The general outcomes of interest are live birth rates and infant abnormalities. Follow-up is measured to confirm successful pregnancy up to successful birth.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Review

Ní Dhonnabháin et al (2022)[5] reported on obstetric outcomes in patients who underwent oocyte, embryo, or ovarian tissue cryopreservation before gonadotoxic therapy and then attempted pregnancy using the cryopreserved cells or tissues (see Table 1 below). A total of 39 case series were included in the final analysis, which included 550 ovarian tissue transplants, 102 embryo transfers (in 75 women), and 178 oocyte transfers (in 170 women). Results of the meta-analysis are found in Table 2. Following the transplant of cryopreserved ovarian tissue, the clinical pregnancy rate was 43.8%, the live birth rate was 32.3%, and the miscarriage rate was 7.5%. A meta-analysis found significantly fewer miscarriages with the use of cryopreserved ovarian tissue compared with cryopreserved embryos (p=.01). Authors noted heterogeneity with regard to surgical techniques across centers.

Table 1. SR & M-A Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Ní Dhonnabháin et al (2022)[5]	Through Nov 2020	39	Patients who underwent oocyte, embryo, or ovarian tissue cryopreservation before gonadotoxic therapy and then attempted pregnancy using the cryopreserved cells or tissues	550 ovarian tissue transplants; 102 embryo transfers (in 75 women); 178 oocyte transfers (in 170 women)	Case series	Not reported

M-A: meta-analysis; SR: systematic review.

Table 2. SR & M-A Results

Study	Clinical pregnancy, %	Live birth, %	Miscarriage, %
Ní Dhonnabháin et al (2022)[5]			
Ovarian tissue cryopreservation	43.8%	32.3%	7.5%
Oocyte cryopreservation	34.9%	25.8%	9.2%
Embryo cryopreservation	49%	35.3%	16.9%
p-value	.09	.11	oocye vs embryo; p=NS ovarian tissue vs embryo; p=.01

CI: confidence interval; M-A: meta-analysis; NS: not significant; SR: systematic review.

Case Series

Cryopreservation of ovarian tissue or an entire ovary with subsequent auto or heterotopic transplant has been investigated as a technique to sustain the reproductive function of women or children who are faced with sterilizing procedures, such as chemotherapy, radiotherapy, or surgery, frequently due to malignant diseases. There are a few case reports assessing the return of ovarian function using this technique.[6] There are also case series describing live births using cryopreserved ovarian tissue.[6] However, in general, the technique is not standardized and insufficiently studied to determine the success rate.[7],[8,] Johnson and Patrizio (2011) commented on whole ovary freezing as a fertility preservation technique in women with disease or disease treatment that threaten their reproductive tract function.[9] They concluded: "Although theoretically optimal from the point of view of maximal follicle protection and preservation, the risks and difficulties involved in whole ovary freezing limit this technique to experimental situations."

Section Summary: Cryopreservation of Ovarian Tissue

As a technique, cryopreservation of ovarian tissue has not been standardized, and there are insufficient published data that this reproductive technique is effective and safe. A systematic review of case series describing patients who underwent oocyte, embryo, or ovarian tissue cryopreservation before gonadotoxic therapy and then attempted pregnancy using the cryopreserved cells or tissue did not identify any significant differences when comparing rates of clinical pregnancy and live birth in patients who used cryopreserved ovarian tissue compared to cryopreserved embryos. However, there were fewer miscarriages with the use of cryopreserved ovarian tissue compared with cryopreserved embryos (7.5% vs 16.9%).

Cryopreservation of Oocytes

Cryopreservation of oocytes has been examined as a fertility preservation option for reproductive-age individuals undergoing cancer treatment. There are 2 primary approaches to

cryopreservation: a controlled-rate, slow-cooling method and a flash-freezing process known as vitrification. Vitrification is faster and requires a higher concentration of cryoprotectants.

Clinical Context and Therapy Purpose

The purpose of cryopreservation of oocytes in individuals with cancer who will undergo treatment that might precipitate infertility is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is cancer individuals who undergo treatment that might precipitate infertility.

Interventions

The therapy being considered is cryopreservation of oocytes.

Comparators

The following practice is currently being used to make decisions about infertility: cryopreservation of embryos but not of ovarian tissue.

Outcomes

The general outcomes of interest are live birth rates and infant abnormalities. Follow-up is measured to confirm successful pregnancy up to successful birth.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

A systematic review by Ní Dhonnabháin et al (2022)[5] is introduced above (see Table 1 above). Included in the final analysis were data from 170 women who underwent 178 oocyte transfers. Results from the meta-analysis are found in Table 2 above. Following the

transplantation of cryopreserved oocytes, the clinical pregnancy rate was 34.9%, the live birth rate was 25.8%, and the miscarriage rate was 9.2%; there were no significant differences when comparing outcomes in patients who used cryopreserved oocytes vs cryopreserved embryos. Authors noted heterogeneity with regard to surgical techniques across centers.

Observational Studies

An Italian database study published subsequent to the joint guidelines compared outcomes in pregnancies achieved with fresh or frozen oocytes.[14] The investigators identified 855 patients who had become pregnant using fresh and/or cryopreserved and thawed oocytes. The authors did not state the reasons for a desire for fertility preservation. Of a total 954 clinical pregnancies; 197 were obtained with frozen oocytes and 757 with fresh oocytes. There were 687 pregnancies from fresh cycle oocytes only, 129 pregnancies with frozen oocytes only, and 138 pregnancies from both fresh and frozen oocyte cycles. The live birth rate was 68% (134/197) from frozen and thawed oocytes and 77% (584/757) from fresh oocyte cycles. The live birth rate was significantly higher after fresh cycle oocytes (p=.008).

Society Recommendations:

The Committee Opinion titled “Fertility preservation in patients undergoing gonadotixic therapy or gonadectomy: a committee opinion” by the Practice Committee of the American Society for Reproductive Medicine (2019)[10] states the following: “Mature oocyte cryopreservation is another strategy for fertility preservation in postpubertal females. This process also requires ovarian stimulation and egg retrieval. Cryopreservation of oocytes rather than embryos allows for greater control of disposition of the individual's gametes in the future and also avoids issues related to embryo disposition, which may be a concern for some patients. Data on pregnancy and live birth rates from oocyte cryopreservation in cancer patients are scarce. One study found a 35% live birth rate in 80 oncofertility patients who returned to use their vitrified oocytes. Age at vitrification and the number of oocytes were predictors of future success[12]. The current data are too limited to determine if oncofertility patients have similar outcomes to elective fertility preservation or donor oocyte patients[12],[13,]. However, in many patients with likelihood of ovarian failure, oocyte vitrification represents the best option for fertility preservation and has resulted in acceptable birth rates.” As supported by ASRM embryo, oocyte, and ejaculated or testicular sperm cryopreservation remain the principle established modalities for fertility preservation. Patients facing treatments likely to impair reproductive function deserve prompt counseling regarding their options for fertility preservation and rapid referral to an appropriate program.

Section Summary: Cryopreservation of Oocytes

There are sufficient published data on the safety and efficacy of cryopreservation of oocytes; data are available from select clinical settings, generally outside of the U.S. A systematic review of case series describing patients who underwent mature oocyte cryopreservation before gonadotoxic therapy and then attempted pregnancy using the cryopreserved cells or tissue did identify improved rates of clinical pregnancy, live birth, and miscarriage in patients who used cryopreserved oocytes compared to cryopreserved embryos. Oocyte cryopreservation may be one of the few options available and therefore is recommended with appropriate counseling.

Cryopreservation of Testicular Tissue in Prepubertal Boys With Cancer

A potential application of cryopreservation of testicular tissue is its potential to preserve the reproductive capacity in prepubertal boys undergoing cancer chemotherapy; cryopreservation of ejaculate is not an option in these patients.

Clinical Context and Therapy Purpose

The purpose of the cryopreservation of testicular tissue in prepubertal boys with cancer is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is prepubertal boys with cancer.

Interventions

The therapy being considered is the cryopreservation of testicular tissue.

Comparators

The following practice is currently being used to make decisions about infertility: no cryopreservation of testicular tissue.

Outcomes

The general outcomes of interest are live birth rates and infant abnormalities. Follow-up is measured in months to confirm successful birth.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Modeling Studies

It has been hypothesized that reimplantation of the frozen-thawed testicular stem cells will reinitiate spermatogenesis or, alternatively, spermatogenesis could be attempted in vitro, using frozen-thaw spermatogonia. While these strategies have been explored in animals, there are inadequate human studies. [5,15,16]

Section Summary: Cryopreservation of Testicular Tissue in Prepubertal Boys With Cancer

No clinical trials were identified evaluating the safety and efficacy of cryopreservation of testicular tissue in prepubertal boys undergoing cancer therapy.

Summary of Evidence

For individuals who have cancer who will undergo treatment that may lead to infertility and who receive cryopreservation of ovarian tissue, the evidence includes case series and a systematic review of case series that have reported on the technique as well as pregnancy and live birth rates after transplantation. The technique used has not been standardized, and there is a lack of controlled studies on health outcomes following cryopreservation of ovarian tissue. The systematic review included data from patients who underwent oocyte, embryo, or ovarian tissue cryopreservation before gonadotoxic therapy and then attempted pregnancy using the cryopreserved cells or tissue. The authors did not identify any significant differences when comparing rates of clinical pregnancy and live birth in patients who used cryopreserved ovarian tissue compared to cryopreserved embryos. However, there were fewer miscarriages with the use of cryopreserved ovarian tissue compared with cryopreserved embryos (7.5% vs 16.9%). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cancer who will undergo treatment that may lead to infertility and who receive cryopreservation of oocytes, the evidence includes RCTs and a systematic reviews assessing the technique in related and target populations. One systematic review found that fertilization rates ranged from 71% to 79%, and the clinical pregnancy rates per transfer ranged from 36% to 61%. The other systematic review included data from case series describing patients who underwent oocyte, embryo, or ovarian tissue cryopreservation before gonadotoxic therapy and then attempted pregnancy using the cryopreserved cells or tissue. The authors did not identify any significant differences when comparing rates of clinical pregnancy, live birth, and miscarriage in patients who used cryopreserved oocytes compared to cryopreserved embryos. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are prepubertal boys with cancer who receive cryopreservation of testicular tissue, the evidence includes no clinical trials evaluating safety and efficacy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

American Society of Clinical Oncology

The American Society of Clinical Oncology (ASCO) first published a clinical practice guideline on fertility preservation for adults and children with cancer in 2006. This guideline was updated in 2013 and in 2018. Recommendations related to preservation of fertility prior to initiating treatment are as [17,18]

- Adult Men:
  Recommendation 2.1. Sperm cryopreservation:
  Sperm cryopreservation is effective, and health care providers should discuss sperm banking with postpubertal males receiving cancer treatment.

  Recommendation 2.2. Hormonal gonadoprotection:
  Hormonal therapy in men is not successful in preserving fertility. It is not recommended.

  Recommendation 2.3. Other methods to preserve male fertility:
  Other methods, such as testicular tissue cryopreservation and reimplantation or grafting of human testicular tissue, should be performed only as part of clinical trials or approved experimental protocols.

- Adult Women:
  Recommendation 3.1. Embryo cryopreservation:
  Embryo cryopreservation is an established fertility preservation method, and it has routinely been used for storing surplus embryos after in vitro fertilization.

  Recommendation 3.2. Cryopreservation of unfertilized oocytes:
  Cryopreservation of unfertilized oocytes is an option and may be especially well suited to women who do not have a male partner, do not wish to use donor sperm, or have religious or ethical objections to embryo freezing.

  Recommendation 3.3. Ovarian transposition:
  Ovarian transposition (oophoropexy) can be offered when pelvic irradiation is performed as cancer treatment. However, because of radiation scatter, ovaries are not always protected, and patients should be aware that this technique is not always successful. Because of the risk of remigration of the ovaries, this procedure should be performed as close to the time of radiation treatment as possible.

  Recommendation 3.5 (updated). Ovarian suppression:
  There is conflicting evidence to recommend GnRHa and other means of ovarian suppression for fertility preservation. The Panel recognizes that, when proven fertility preservation methods such as oocyte, embryo, or ovarian tissue cryopreservation 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. However, GnRHa should not be used in place of proven fertility preservation methods.

American Society of Reproductive Medicine
Fertility Preservation in Patients Undergoing Gonadotoxic Therapy or Gonadectomy: A Committee Opinion (2019)[10]
The ASRM 2019 committee opinion summarizes programmatic requirements for comprehensive fertility-preservation care and provides specific clinical recommendations based on current practice. Strategies for adult females include ovarian stimulation, embryo cryopreservation, mature oocyte cryopreservation and ovarian transposition. Strategies for adult males include ejaculated sperm cryopreservation and cryopreservation of surgically extracted sperm.

- Embryo, oocyte, and ejaculated or testicular sperm cryopreservation remain the principle established modalities for fertility preservation.
- Ovarian tissue cryopreservation is no longer considered experimental and can be used in prepubertal patients or when there is not time for ovarian stimulation.
- Testicular tissue cryopreservation in prepubertal males is still considered experimental and should be conducted under research protocols when no other options are feasible.

Government Regulations

National: There are no documents related to preservation of fertility.

Local: There are no documents related to preservation of fertility.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

Assisted Reproductive Techniques
Genetic Testing - Preimplantation
Infertility Diagnosis

References

1. Practice Committee of the American Society for Reproductive Medicine, American Society for Reproductive Medicine, (2023 by American Society for Reproductive Medicine.) FNS_ASRM_Reviewers_proof 1..1 assessed 4/17/24
2. Ethics Committee of the American Society for Reproductive Medicine. Fertility preservation and reproduction in patients facing gonadotoxic therapies: an Ethics Committee opinion. Fertil Steril 2018;110(3):380-386.
3. Alliance for Fertility Preservation. State laws & legislation. Updated 3/20/24. https://www.allianceforfertilitypreservation.org/state-legislation/ Accessed 4/17/24.
4. Ethics Committee of the American Society for Reproductive Medicine. Fertility preservation and reproduction in patients facing gonadotoxic therapies: an Ethics Committee opinion. Fertil Steril 2018;110(3):380-386.
5. Ni Dhonnabhain B, Elfaki N, Fraser K, et al. A comparison of fertility preservation outcomes in patients who froze oocytes, embryos, or ovarian tissue for medically indicated circumstances: a systematic review and meta-analysis. Fertil Steril. Jun 2022; 117(6): 1266-1276. PMID 35459522
6. Wiemer KE, Cohen J, Tucker MJ, et al. The application of co-culture in assisted reproduction: 10 years of experience with human embryos. Hum Reprod. Dec 1998; 13 Suppl 4: 226-38. PMID 10091073
7. Tryde Schmidt KL, Yding Andersen C, Starup J, et al. Orthotopic autotransplantation of cryopreserved ovarian tissue to a woman cured of cancer - follicular growth, steroid production and oocyte retrieval. Reprod Biomed Online. Apr 2004; 8(4): 448-53. PMID 15149569
8. Oktay K, Buyuk E, Veeck L, et al. Embryo development after heterotopic transplantation of cryopreserved ovarian tissue. Lancet. Mar 13 2004; 363(9412): 837-40. PMID 15031026
9. Johnson J, Patrizio P. Ovarian cryopreservation strategies and the fine control of ovarian follicle development in vitro. Ann N Y Acad Sci. Mar 2011; 1221: 40-6. PMID 21401628
10. Practice Committee of the American Society for Reproductive Medicine. Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. Fertil Steril 2019;112(6): 1022-1033. PMID 31843073 Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion (2019) | American Society for Reproductive Medicine | ASRM Accessed 4/17/24.
11. A Cobo and others, Elective and Onco-fertility preservation: factors related to IVF outcomes, *Human Reproduction*, Volume 33, Issue 12, December 2018, Pages 2222–2231, https://doi.org/10.1093/humrep/dey321 assessed 4/17/24
12. Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. Mature oocyte cryopreservation: a guideline. Fertil Steril. Jan 2013; 99(1): 37-43. PMID 23083924
13. Cobo A, Garrido N, Pellicer A, Remohí J. Six years' experience in ovum donation using vitrified oocytes: report of cumulative outcomes, impact of storage time, and development of a predictive model for oocyte survival rate. Fertil Steril. 2015 Dec;104(6):1426-34.e1-8. doi: 10.1016/j.fertnstert.2015.08.020. Epub 2015 Sep 6. PMID: 26353081.

14. Levi Setti PE, Albani E, Morenghi E, et al. Comparative analysis of fetal and neonatal outcomes of pregnancies from fresh and cryopreserved/thawed oocytes in the same group of patients. Fertil Steril. Aug 2013; 100(2): 396-401. PMID 23608156
15. Hovatta O. Cryobiology of ovarian and testicular tissue. Best Pract Res Clin Obstet Gynaecol. Apr 2003; 17(2): 331-42. PMID 12758103
16. Tournaye H, Goossens E, Verheyen G, et al. Preserving the reproductive potential of men and boys with cancer: current concepts and future prospects. Hum Reprod Update. Nov-Dec 2004; 10(6): 525-32. PMID 15319377
17. Loren AW, Mangu PB, Beck, LN, et al. Fertility preservation for Patients with Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. Journal of Clinical Oncology. 2013. July;31(19):2500-2511. Fertility Preservation for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update | Journal of Clinical Oncology (ascopubs.org) assessed 4/17/24
18. Loren, AW, Mangu PB, Beck LN, et al. Fertility Preservation for Patients with Cancer: ASCO Clinical Practice Guideline Update. Journal of Clinical Oncology. 2018. July;36:19 (10);1994-2001. PMID 29620997. Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update Summary | JCO Oncology Practice (ascopubs.org) Assessed 4/17/24

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 4/17/24, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
7/1/22	4/19/22		Joint policy established
9/1/22	6/21/22		Removal of age limits for biological female individuals. Exclusions: added post-menopausal females. Minor verbiage edits.
9/1/23	6/13/23		Routine Maintenance (jf) Vendor Managed: NA • 89398 added as investigational *To clarify this code is for cryopreservation of ovarian tissue* • 89344, 89354, 89335 added as E/I • Added from BCBSA 4.02.04 - Reproductive Techniques September 2022. Added PICO's With cancer who will undergo treatment that may lead to infertility and who are prepubertal boys with cancer. Added PICO Cryopreservation of Oocytes and Cryopreservation of ovarian tissue. Ref removed since no longer current references in policy 7,8,15-19 -Added ref 12,13,14,15 added from 2019 version Practice Committee of the American Society for Reproductive Medicine. Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion - Under inclusions to add two from one on thawing and storage. • Added under exclusions: Cryopreservation of ovarian tissue, immature oocytes, and testicular tissue in pubertal boys. • Cryopreservation of testicular tissue in pre pubertal boys (biologic) males.

9/1/24	6/11/24		Routine Maintenance (jf) Vendor Managed: NA Ref: 1 updated, 2 removed

Next Review Date: 2nd Qtr, 2025

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: INFERTILITY RELATED TO CANCER TREATMENT

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered, criteria apply
BCNA (Medicare Advantage)	See Government Regulations section of the policy.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.
- Duplicate (back-up) equipment is not a covered benefit.