Medical Policy Reference Manual
Medical Policy

4.02.001 Assisted Reproductive Technology (ART) Procedures: In Vitro Fertilization (IVF) Gamete Intrafallopian Transfer (GIFT) Zygote Intrafallopian Transfer (ZIFT)

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Description

Assisted reproductive technology (ART) procedures are complex treatments for infertility. **Infertility** is the inability to conceive after 1 year of unprotected vaginal intercourse, or as otherwise defined by the law. Included among the ART procedures are in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT), and zygote intrafallopian transfer (ZIFT).

Each of these procedures includes a series of services performed over a limited period of time known as a **cycle**. *A cycle is defined as 1 attempt at conception, and covers a range of services which includes, but is not limited to, ultrasounds, medications, medical visits, laboratory testing, and surgical procedures that are medically necessary to complete the ART attempt and that are not otherwise excluded (i.e., experimental/ investigational).*

- IVF involves stimulation of the ovaries with exogenous hormones, retrieval of oocytes/ova (eggs), fertilization of the oocytes in a petri dish, and the transfer of any resulting embryo(s) back into the uterus.
- GIFT involves the injection of sperm directly into the fallopian tube during laparoscopy, following stimulation of the ovaries with exogenous hormones. The goal is for fertilization to occur naturally in vivo, so that pregnancy will be achieved.
- ZIFT combines steps from both IVF and GIFT. In ZIFT, the oocytes are fertilized outside the body (as in IVF), and the resultant early embryos (zygotes) are injected directly into the fallopian tubes during laparoscopy (as in GIFT).

The various components of ART and transfer into the uterus can be broadly subdivided into oocyte harvesting procedures, which are performed on the female partner; sperm collection procedures, which are performed on the male partner; and the in vitro component (i.e., the laboratory procedures) which are performed on the collected oocyte and sperm. The final step is the transfer procedure. Not all steps are routinely done in each case.

Related ART and Laboratory Procedures:

- Fine needle aspiration biopsy, including ultrasound guidance first lesion; each additional lesion
- **Fine needle aspiration**; without imaging guidance first lesion; each additional lesion
- **Biopsy of testis**, needle (separate procedure)
- **Biopsy of testis,** incisional (separate procedure)
- **Biopsy of epididymis**, needle
- **Electroejaculation**
- **Follicle puncture for oocyte retrieval**, any method
- **Embryo transfer**, intrauterine
- **Gamete, zygote, or embryo intrafallopian transfer**, any method (i.e., GIFT or ZIFT)
- **Estradiol, total**
- **Gonadotropin**; **follicle stimulating hormone** (FSH)
- **Gonadotropin**; **luteinizing hormone** (LH)
- **Progesterone**
- **Gonadotropin, chorionic** (hCG); quantitative
- **Culture of oocyte(s)/embryo(s),** less than 4 days

- **Culture of oocyte(s)/embryo(s), less than 4 days; with co-culture of oocyte(s)/embryos**. Co-culture techniques involve tissue culture of human oocyte(s)/embryos in the presence of oviductal, uterine, granulosa, or other cells. The procedure involves the isolation of the substrate cells, culture, plating, and co-culture of these cells with human oocyte(s)/embryos. The purpose of co-culture is to produce a more viable embryo for subsequent transfer to the uterus. Co-culture is not routinely done as part of all IVF procedures; the technique may not be available in all infertility labs.

- **Assisted embryo hatching, micro techniques, any method**. Assisted hatching is a technique performed to enhance the likelihood that the transferred embryo will implant in the uterus and establish a viable pregnancy. The technique involves in vitro disruption of the zona pellucida surrounding the embryo so that the embryo can "escape" and implant into the uterine wall. Assisted hatching has also been referred to as zona drilling and partial zonal dissolution. Assisted hatching is commonly performed as part of an IVF procedure in women over 40 who have a decreased incidence of implantation after embryo transfer and in women with prior failed IVF cycles due to failed implantation.

- **Oocyte identification from follicular fluid**. As part of the oocyte retrieval procedure, follicular fluids are provided to the laboratory. Using microscopic examination and dissection, the oocytes are identified, isolated, classified, and placed in the culture environment.

- **Preparation of embryo/blastocyst for transfer (any method).** Embryos resulting from ART techniques must be evaluated microscopically for stage of development, cell number, and quality in order to select the optimal embryo(s) for transfer. The selected embryos are loaded into an embryo transfer catheter, which is introduced by a physician into a patient's uterus or fallopian tubes. Following the transfer, the catheter is flushed, and the flushings are examined to determine if the embryo(s) have been successfully transferred.

- **Sperm identification from aspirate, (other than seminal fluid).** After aspiration of sperm from the epididymis or testis, the fluid undergoes immediate laboratory analysis so that the sperm can be identified and isolated.

- **Cryopreservation; embryo(s).** Cryopreservation involves moving the embryo through increasing concentrations of cryoprotectant and loading the embryo into straws or vials for subsequent freezing. The embryos are cooled gradually and then stored for as long as needed. It is estimated that about 20% of couples undergoing ART procedures would have embryos frozen.

- **Cryopreservation of oocyte(s);** Oocytes (eggs) may be frozen using methods that include ultrarapid freezing (vitrivication) which optimizes oocyte survival.

- **Cryopreservation; sperm**, **testicular tissue.** Sperm are assessed for pre-freeze concentration, motility, and viability, followed by addition of cryoprotectant agent. Aliquots are loaded into straws or vials, and the sample is cooled and stored. Cryopreservation is indicated for any diagnosis where chemical or surgical castration is considered appropriate, or in other circumstances that preclude the collection of a semen sample on demand (examples: paraplegia, ejaculatory dysfunction), following electroejaculation or sperm aspiration, prior to a vasectomy, or in situations in which the male must be absent for long periods of time (examples: military service).

- **Sperm isolation: simple prep** (e.g., sperm wash and swim up) for insemination or diagnosis with semen analysis)

- **Sperm isolation; complex prep** (examples: Percoll gradient, albumin gradient) for insemination or diagnosis with semen analysis. Simple or complex sperm isolation may be performed prior to intrauterine insemination or IVF. The choice of simple or complex preparation is based on a prior semen analysis.

- **Sperm identification from testis tissue,** fresh or cryopreserved.

- **Insemination of oocytes**.

- **Extended culture of oocytes/embryo(s), 4-7 days.** Culturing beyond 4 days allows the embryo to develop to the blastocyst stage

- **Assisted oocyte fertilization, microtechnique; less than or equal to 10 oocytes.** Microtechnique fertilization refers to intracytoplasmic sperm injection (ICSI).

- **Assisted oocyte fertilization, microtechnique; greater than 10 oocytes**. Microtechnique fertilization refers to intracytoplasmic sperm injection (ICSI).

- **Storage of embryo(s);** sperm/semen; testicular tissue; or oocyte(s)

- **Thawing of cryopreserved;** embryo(s)

- **Thawing of cryopreserved oocyte(s)**, each aliquot

- **Thawing of cryopreserved, sperm/semen, each aliquot;** testicular tissue

- **S4011**: **In vitro fertilization**: including but not limited to identification and incubation of mature oocytes, fertilization with sperm, incubation of embryo(s), and subsequent visualization for determination of development. (The following procedures would be included in the S4011 code: Culture of oocyte(s)/embryo(s), less than 4 days, oocyte identification from follicular fluid, sperm isolation; simple prep, and insemination of oocytes

Policy

NOTE: Certain contracts contain specific wording with regard to coverage of this service. Benefits provided by the member's contract supersede the statements of Medical Policy. In the event the contract does not address these services, this Medical Policy applies. Therefore, one should refer to the contract language to be certain of limitations of coverage prior to quoting benefits, adjudicating claims, preauthorizing, or performing treatment.

Coverage eligibility of ART is a contract-specific benefit issue. Cryopreservation, storing and thawing of mature oocyte(s), embryo(s) is considered medically necessary only when the member is about to undergo gonadotoxic treatment such as chemotherapy or radiation.

- When benefits are available, the appropriate procedure noted above, where applicable, may be included with the following exceptions:

- Co-culture of oocyte(s)/embryo(s) is considered **experimental / investigational,** as it does not meet TEC criteria # 2, 3, and 5.

- Cryopreservation of ovarian tissue is considered **experimental / investigational**, as it does not meet TEC criteria # 2 and 3.

- Cryopreservation of testicular tissue in prepubertal boys is considered **experimental / investigational,** as it does not meet TEC criteria # 2, 3, and 5.

- Storage and thawing of testicular tissue in prepubertal boys are considered **experimental / investigational**, based on the fact that the cryopreservation of testicular tissue is considered **experimental / investigational.**

- Cryopreservation of immature oocytes is considered **experimental / investigational**, as it does not meet TEC criteria #2, 3, and 5.

- Storage and thawing of ovarian tissue are considered **experimental / investigational**, based on the fact that the cryopreservation of ovarian tissue is considered **experimental / investigational.**

- Sperm evaluation, Hyaluronan sperm binding test is considered **experimental / investigational**, as it does not meet TEC criteria # 2-5.

- The sperm acrosome reaction test is considered **experimental / investigational** as it does not meet TEC criteria # 2 - 5.

Policy Guidelines

Experimental/Investigational

The term "experimental/investigational" describes services or supplies that are in the developmental stage and are in the process of human or animal testing. Services or supplies that do not meet all 5 of the criteria listed below adopted by the BlueCross BlueShield Association (BCBSA) Medical Policy Services (MPS) Assessment Criteria (formerly known as the TEC Criteria or "Technology Evaluation Center") criteria are deemed to be experimental/investigational:

1. The technology* must have final approval from the appropriate U.S. government regulatory bodies; and
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes; and
3. The technology must improve the net health outcome; and
4. The technology must be as beneficial as any established alternatives; and
5. The improvement must be attainable outside the investigational settings.

* Technology includes drugs, devices, processes, systems, or techniques

Rationale:

A review of available peer-review literature does not support the effectiveness of cryopreservation of ovarian tissue and oocytes. There are few case studies concerning the cryopreservation of ovarian tissue, with subsequent autotransplantation, in an attempt to preserve the possibility of future fertility, prior to receiving radiation or chemotherapy; however, there have been few successful outcomes. Presently, the technique is not standardized. It has been investigated more thoroughly in animal models but has not been widely applied to humans.

A scarcity of peer-review literature exists regarding embryo co-culture techniques. This technique represents an effort to improve the culture media for embryos; however, no standardized method of co-culture has emerged, and no controlled trials have evaluated an improved implantation or pregnancy rate associated with co-culture.

According to the American Society for Reproductive Medicine, cryopreservation of ovarian tissue and oocytes remain experimental / investigational and should only be offered in a research setting. The American Society of Clinical Oncology states that sperm and embryo cryopreservation is considered standard practice and is a widely accepted practice; however, other available fertility preservation methods (example: cryopreservation of ovarian tissue and oocytes) remain experimental/ investigational until further research proves otherwise.

2021 Update:

A search of peer reviewed literature was performed for the period of November 2018 through December 2020. According to the ASRM (2019), ovarian tissue banking is an acceptable fertility-preservation technique and is no longer considered experimental. Overall, 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. Embryo, oocyte, and ejaculated or testicular sperm cryopreservation remain the principle established modalities for fertility preservation. Testicular tissue cryopreservation in prepubertal males is still considered experimental and should be conducted under research protocols when no other options are feasible.

In the Journal Pediatrics (Klipstein, 2020), it is written currently ovarian tissue cryopreservation is only available in certain parts of the United States as an open clinical trial to assess its efficacy and safety as a potential option for preservation of fertility in prepubertal girls. Within this context, it is the only method that can be offered to prepubertal girls. This technique has been performed in children as young as 2.7 years of age, and the chance of later restoring fertility should theoretically be higher because the ovarian cortex contains more primordial and primary follicles in younger children. Ideally, the stored ovarian tissue is thawed and autotransplanted into the donor once her treatment has been completed. There is no data yet available regarding whether cryopreservation of ovarian tissue in prepubertal girls can lead to pregnancy and delivery. Given the potentially limited viability of the autotransplanted tissue, this procedure is more likely to restore reproductive endocrine function rather than result in preserving fertility. Given the unknown efficacy of this technique, ovarian tissue cryopreservation in prepubertal girls is best performed under an IRB protocol.
Findings in the recent literature do not change the conclusions regarding the current standards of practice for assisted reproductive technology procedures. Therefore, the policy statements are unchanged.

2018 Update:
A search of peer reviewed literature was performed for the period of November 2016 through October 2018. Findings in the recent literature do not change the conclusions regarding the current standards of practice for assisted reproductive technology procedures, and the use of cryopreservation of ovarian tissue as investigational. Therefore, the policy statements are unchanged.

2016 Update:
A search of peer reviewed literature was performed for the period of October 2014 through October 2016. The American Society for Reproductive Medicine (ASRM) recommends mature oocyte cryopreservation for patients facing infertility due to chemotherapy or other gonadotoxic therapies. ASRM no longer considers cryopreservation as experimental, however, does not recommend cryopreservation for healthy patients. The ASRM continues to consider cryopreservation of ovarian tissue as experimental. Cryopreservation of oocyte(s), embryo(s) is a contract-specific benefit issue.

2014 Update:
In a 2013 committee opinion, the American Society for Reproductive Medicine (ASRM) no longer deems oocyte cryopreservation an experimental procedure for post pubertal females facing infertility as the result of pelvic radiation therapy and chemotherapy as they are gonadotoxic therapies. The American Society of Clinical Oncology Clinical Practice Guideline Update (2013) relating to fertility preservation in patients with cancer, clarified that sperm and embryo cryopreservation as well as oocyte cryopreservation are considered standard practice and are widely available as methods of fertility preservation. The American College of Obstetricians and Gynecologists' (ACOG) Committee on Gynecologic Practice in a 2014 Committee Opinion, endorsed the 2013 ASRM statement and encouraged the use of ovarian cryopreservation by its Fellows for post pubertal females facing infertility as the result of cancer treatments. ACOG notes "there are not yet sufficient data to recommend cryopreservation for the sole purpose of circumventing reproductive aging in healthy women."

2012 Update:
A search of peer reviewed literature was performed for the period of October 2008 through January 2012. Findings in the literature do not change the conclusions regarding the current standards of practice for assisted reproductive technology procedures.

2008 Update:
A search of peer-reviewed literature was performed for the period of September 2006 through September 2008. Findings in the recent literature do not change the conclusions regarding the procedures noted in the policy section; therefore, the policy statements remain unchanged.

Benefit Applications

- **Trial (mock) embryo transfer:** Separate benefits are not provided for trial (mock) embryo transfer, as it is considered an integral part of the embryo transfer, intrauterine, procedure. Report trial (mock) embryo transfer with "unlisted procedure, female genital system."

- **Preparation of blastocyst/embryo for transfer**: Separate benefits may be provided for preparation of the embryo for transfer when the provider of the service is not employed by the facility.

- **Culture of oocyte(s)/embryo(s), less than 4 days**; extended culture of oocyte(s)/embryo(s), 4-7 days: Benefits are provided for culture of oocytes (embryo or blastocyst). NOTE: Reported one time per treatment cycle only, regardless of the number of oocytes.

Refer to the member's contract for specific benefits regarding all of the following:
- Eligibility
- Donor sperm/oocytes/embryo
- Charges related to sperm and semen analysis and preparation
- Medications
- Embryo thawing
- Thawing of cryopreserved sperm/semen, testicular tissue, oocytes, each aliquot
- Cryopreservation of embryo/sperm
- Cryopreservation, mature oocyte(s)
- Storage of cryopreserved sperm, semen, testicular tissue, embryos, or oocyte(s)
- Surrogacy

- Elective reversal of male sterility
- Elective reversal of female sterility

Contracts which follow **Maryland state mandates** are required to provide certain benefits for IVF, according to the guidelines below. Other Plan contracts must have a benefit for the specific ART procedure requested (examples: IVF, GIFT, or ZIFT). Check the individual contract for specific benefits. **When the contract does not include coverage for ART, benefits are not provided for any of the services related to the ART procedure.**

Maryland State Mandate Guidelines (Md Code Ann. Ins. §15-810)

CareFirst may limit coverage to three attempts per live birth. (An *attempt* is the equivalent to a *cycle,* as defined in the Definition section of this procedure.) CareFirst requires a Certificate of Live Birth, if necessary, in order to make a determination that the condition of this benefit has been met.

- The entire IVF benefit is subject to a $100,000 lifetime benefit maximum and no benefits are available for IVF services after the maximum has been reached.
- The member may have any combination of GIFT, ZIFT and IVF counted toward the three attempts allowed per live birth (examples: three IVF procedures, and a live birth; two GIFT procedures and one IVF procedure, and a live birth; one IVF, one GIFT, and one ZIFT procedure, and a live birth, etc.).
- If a member has a partial attempt (or cycle) (examples: fertility drugs, laboratory testing, oocyte retrieval) including all procedures up to the actual transfer, but does not have the actual transfer, the incomplete attempt (or cycle) will not be counted towards the three attempts allowed per live birth. The associated costs for incomplete attempts (or cycles) will be counted towards the $100,000 lifetime benefit maximum.

For contracts which follow Maryland state mandates, benefits **are provided** when ***all*** of the following criteria are met:

1. the patient is the policyholder or subscriber or a covered dependent of the policyholder or subscriber; and

2. for a married patient whose spouse is of the opposite sex[2], the patient's oocytes (eggs) are fertilized with the patient's spouse's sperm, unless:

-- the patient's spouse is unable to produce and deliver functional sperm; and

-- the inability to produce and deliver functional sperm does not result from:

a. a vasectomy; or
b. another method of voluntary sterilization, [4] and

3. for a married patient, the patient and the patient's spouse have a documented history of involuntary infertility or a diagnosed medical condition which may be demonstrated by a history of:

-- if the patient and the patient's spouse are of opposite sex, intercourse of at least one year[5] duration failing to result in pregnancy; or

-- if the patient and the patient's spouse are of the same sex[2], three attempts of artificial insemination over the course of 1 year failing to result in pregnancy[5] or

-- the infertility of the patient or the patient's spouse is associated with any of the following diagnosed medical conditions[2]:

a. endometriosis.
b. exposure in utero (before birth) to diethylstilbestrol, commonly known as DES.
c. blockage of, or surgical removal of, one or both fallopian tubes (lateral or bilateral salpingectomy) (excluding tubal blockage due to a previous elective sterilization); or
d. abnormal male factors including oligospermia, contributing to the infertility (excluding previous elective sterilization)[3], ***and***

4. For an unmarried patient: The patient has had three attempts of artificial insemination over the course of 1 year failing to result in pregnancy; or

The infertility is associated with any of the following medical conditions of the patient:

a. endometriosis.
b. exposure in utero (before birth) to diethylstilbestrol, commonly known as DES.
c. blockage of, or surgical removal of, one or both fallopian tubes (lateral or bilateral salpingectomy) (excluding tubal blockage due to a previous elective sterilization); or
d. abnormal male factors including oligospermia, contributing to the infertility (excluding previous elective sterilization) [3] ***and***

5. the patient has been unable to attain a successful pregnancy through a less costly infertility treatment for which coverage is available under the policy or contract; ***and***

6. the in vitro fertilization procedures are performed at medical facilities that conform to applicable guidelines or minimum standards issued by the American College of Obstetricians and Gynecologists (ACOG) guidelines for in vitro fertilization clinics or the American Society for Reproductive Medicine (ASRM), (formerly the American Fertility Society) minimal standards for programs of in vitro fertilization.

Effective January 1, 2019, to provide coverage for "standard fertility preservation procedures", including sperm and oocyte cryopreservation and evaluations, laboratory assessments, medications, and treatments associated with sperm and oocyte cryopreservation, that are (1) performed on a policyholder or subscriber or on the dependent spouse of a policyholder or subscriber (2) medically necessary to preserve fertility due to a need for medical treatment that may directly or indirectly cause "iatrogenic infertility." Pursuant to Maryland State mandate S.B. 271 H.B 908 effective 01/01/2019.

[1] Decreased from 5 years, effective 10/01/2000, according to Maryland S.B. 516. **NOTE:** Benefit is effective for new risk contracts as of 10/01/2000. For contracts which are renewed on or after 10/01/2000, a benefit is provided on the date the contract is renewed.

[2] Updated coverage for same sex couples according to Maryland State mandate S.B 416 H.B. 838 effective 07/01/2015

[3] Male factor infertility was added to the Maryland State mandate in 2000, effective 10/01/2000.

NOTE: Benefit is effective for new risk contracts as of 10/01/2000. For contracts which are renewed on or after 10/01/2000, a benefit is provided on the date the contract is renewed.

Male factor infertility includes the following:
Mechanical Infertility
- antegrade or retrograde ejaculation, ejaculation failure
Immunological
- anti-sperm antibodies
- unilateral testicular obstruction with auto-immune oligospermia
Abnormal semen quality (volume, motility, concentration, pH, morphology, WBCs)
- oligoasthenoteratozoospermia (OAT syndrome)
- idiopathic, environmental, acquired, genetic, iatrogenic, systemic disease, immunological, occupational
- may be related to varicocele, smoking, alcoholism, exposure to pesticides, radiation, etc.
Occult sperm dysfunction

Note: Male factor infertility also generally includes such factors as azoospermia; however, azoospermia, when due to failure of spermatogenesis, is not included in the state mandate definition because it does not meet the mandate's benefit requirement.

[4] Updated coverage for in vitro fertilization, use of spouse's sperm - exception - pursuant to Maryland State mandate S.B 1 H.B. 11 effective July 1, 2016.

[5] Decreased from two years and six attempts effective 01/01/2021, according to Maryland H.B. 781. This benefit applies to all policies, contracts, and health benefit plans issued, delivered, or renewed in the State of Maryland on or after January 1, 2021.

Certain contracts may have specific limitations regarding the number of allowed attempts or a dollar amount maximum for these services. The Maryland state mandate stipulates a $100,000 lifetime benefit maximum.

Carriers are not responsible for any costs incurred by a policyholder, subscriber, or dependent in obtaining donor sperm.

NOTE: For FEP, check the member's contract for benefits.

Provider Guidelines

Prior authorization may be required for ART services. Check the member's contract to determine if prior authorization is required for ART services. **Before initiating a request for authorization of services, benefits must be verified.** Contact the customer service number on the back of the member's card to determine if the member has benefits for the planned services.

If benefits exist, the following information must be submitted for review when prior authorization is required for infertility services:

- A completed *Assisted Reproductive Technology Pre-Treatment Form.* Incomplete forms will delay the authorization process. This form may be obtained on the CareFirst website at www.carefirst.com/providers.

- Office notes and other medical documentation include a detailed history to confirm the diagnosis of infertility and its duration and cause. Reports of lab work (examples; Estradiol, Serum Progesterone, FSH, postcoital testing, semen analysis) and other related procedures (examples; hysterosalpingography, laparoscopy, endometrial biopsy) may be requested.

- The above clinical information MUST be faxed to Preservice Review Fax: 410-720-3060 or mailed to: CareFirst BlueCross BlueShield, Preservice Review Department, 1501 S. Clinton Street, 8th Floor, Mail Stop CT-08-02, Baltimore, Md. 21224.

- Providers can also request prior authorization electronically by doing the following:

  - If the provider is already registered for CareFirst Direct:
  - Log in at www.carefirst.com/provider/login.
  - Click the Prior Auth/Notifications tab to begin your request.
  - If the provider is not yet registered for CareFirst Direct:
  - Go to www.carefirst.com/provider.
  - Click Register Now.

- Once services are approved, providers will need to obtain separate authorization for infertility medication.

Cross References to Related Policies and Procedures

4.02.007	Preimplantation Genetic Testing, Policy
4.02.009	Assisted Reproductive Technology (ART): Artificial Insemination (AI)/Intrauterine Insemination (IUI), Medical, Policy
11.01.009	Hypo-osmotic Swelling Test for Sperm Function, Policy
11.01.013	Archived Sperm Evaluation, Hamster Penetration Test, Policy
11.01.015	Preconception Sex Selection Techniques, Policy

References

The following were among the resources reviewed and considered in developing this policy. By reviewing and considering the resources, CareFirst does not in any way endorse the contents thereof nor assume any liability or responsibility in connection therewith. The opinions and conclusions of the authors of these resources are their own and may or may not be in agreement with those of CareFirst.

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