KAISER PERMANENTE® **Northwest Region Utilization Review**

UR 68: Assisted Reproductive Technology (ART) Medical Necessity Criteria

Department: Non-Behavioral Health	Number: UR 68
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Review Responsibility: Peter Miksovsky, MD, OB/GYN	Last Revised: 4/23, 4/24, 11/24, 1/26

ASSISTED REPRODUCTIVE TECHNOLOGY MEDICAL NECESSITY CRITERIA

DEFINITIONS

ART- Assisted Reproductive Technology refers to procedures in which pregnancy is attempted through the manipulation of sperm and egg outside the body, such as in vitro fertilization (IVF) or gamete intra-fallopian transfer (GIFT).

IVF- In-vitro fertilization involves retrieving an egg from the woman, combining with sperm in a lab, observing and raising the embryos in the lab for 3 to 5 days, then transferring the resulting embryo back into her uterus.

GIFT- gamete intra-fallopian transfer is a modified version of in vitro fertilization (IVF). GIFT involves retrieving an egg from the woman, combining with sperm in a lab then immediately transferring the unfertilized egg and sperm into her fallopian tube with fertilization taking place in the fallopian tube instead of in a laboratory dish.

ZIFT- zygote intra-fallopian transfer is a modified version of in vitro fertilization (IVF). ZIFT involves retrieving an egg from the woman, combining with sperm in a lab then transferring the fertilized egg (called a zygote) into her fallopian tube before cell division takes place. The zygote is transferred the next day after fertilization occurs.

IUI- Intra-uterine insemination is the placement of washed and concentrated sperm via a catheter into a woman's uterus when she is ovulating. It is often combined with superovulation medicine to increase the number of available eggs, which can result in multiple gestation.

POLICY AND CRITERIA

Coverage guidance: ART may be excluded from coverage. Check CM for exclusions or limitations.

Source	Policy
For Medicare Members	
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	None
Local Coverage Determinations (LCD)	None
Local Coverage Article	None
Kaiser Permanente Medical Policy for Medicare Members	UR 68 applies. Due to the absence of a NCD or LCD, Kaiser Permanente has chosen to use their own Clinical Review Criteria, "Assisted Reproductive Technology" for medical necessity determinations.

For Medicaid Members	
OR Medicaid	UR 68 does not apply. Check Linefinder
WA Medicaid	UR 68 does not apply
Commercial and Self Funded Members	
OR Commercial	UR 68 applies
WA Commercial	UR 68 applies
Self-funded plans	UR 68 applies

Assisted reproductive technology may be indicated when the following criteria are met:

- Referred by KP OB/GYN or Urology or equivalent network provider; AND
- No history of prior in vitro fertilization cycle, OR maximum number of prior in vitro fertilization cycles has not exceeded a total of 6 cycles without a live birth; AND
- Patient or partner meets ANY of the following:
    - Individual is assigned female at birth (AFAB) and aged 40 and older; OR
    - Individual is AFAB aged less than 40 years; AND any of the following:
        - has WHO class 1 or 2 anovulation AND has completed a trial of letrozole between 7.5mg – 10mg (or clomiphene citrate up to 150mg if letrozole cannot be tolerated) or injectable gonadotropins and did not ovulate; OR has WHO class 3 (hypergonadotropic hypoestrogenic) anovulation; OR
        - has hysterosalpingogram (HSG) indicating bilateral blocked or nonpatent fallopian tubes (e.g., due to prior ectopic pregnancy, pelvic inflammatory disease, distal tubal occlusions, hydrosalpinx, other causes); OR
        - has unilateral distal tubal occlusion and no hydrosalpinx AND initial treatments are unsuccessful (i.e., after 4 ovulatory cycles in previously anovulatory patients or after 4 IUI cycles in patients with otherwise unexplained infertility); OR
        - has AMH test results of 0.99 ng/ml or less; OR
        - has had treatment for infertility due to any one of the following AND infertility treatment has been unsuccessful:
            - Endocrinopathy (e.g., hypothyroidism, adrenal disorders, pituitary tumor; OR
            - Endometriosis; OR
            - Intrauterine pathology (e.g., adhesions, polyps, submucosal leiomyomas); OR
            - Pelvic adhesions; OR
            - Polycystic ovarian syndrome, AND:
                - Other causes of infertility ruled out or treated (e.g., thyroid disease, hyperprolactinemia, male factor infertility in partner); AND
                - Treated with at least 6 cycles of letrozole or clomiphene citrate; OR
            - Tubal anastomosis (i.e., reversal of tubal ligation); OR
        - diagnosed with unexplained infertility, AND:
            - Age 37 years and younger and has had at least 3 cycles of IUI with clomiphene citrate or letrozole; OR
            - Age 38 and older; OR

- is undergoing donor IUI and has had 3 or more unsuccessful cycles; OR
- Individual is assigned male at birth (AMAB); AND any of the following:
  - has total motile sperm count (TMSC) less than 10 million in semen analysis after urological evaluation (and intervention, if indicated per urologist); OR is attempting IUI and post-wash TMSC is <1 million on 2 or more occasions; OR
  - Has nonobstructive azoospermia or severe oligospermia; OR
  - Has hypogonadotropic hypogonadism; OR
  - Has paraplegia, necessitating sperm retrieval to achieve pregnancy (e.g., electro-ejaculation or surgical sperm retrieval); OR
- Individual or their partner with infertility or impending infertility due to medical or surgical treatment (e.g., chemotherapy, radiotherapy, gonadotoxic medication, oophorectomy, orchiectomy) or medical condition (e.g., Klinefelter syndrome or Turner syndrome); AND
  - Patient had embryo, oocyte, or sperm cryopreservation prior to treatment or patient is supplying donor gametes or embryos.

SPECIAL GROUP CONSIDERATIONS

OR PEBB- Check fertility benefit with each request as to whether females must be diagnosed as *infertile* to qualify for infertility treatment.

Cryopreservation is typically excluded from coverage unless the member has coverage for ART, in which case, the short-term cryopreservation associated with an ART cycle is also covered. Long-term storage and cryopreservation outside of an ART cycle is typically not covered unless a group has elected the iatrogenic buy-up.
The Exclusion is applied when cryopreservation is requested/billed as a distinct procedure aside from a covered ART procedure.
When cryopreservation is covered, procedures to obtain eggs/sperm are also covered.

RATIONALE

EVIDENCE BASIS

MCG reviewed the evidence on assisted reproductive technology (ART) in 2022. Their findings are provided below:

For infertility, evidence demonstrates a net benefit, but of less than moderate certainty, and may consist of a consensus opinion of experts, case studies, and common standard care. Guidelines recommend mature oocyte, embryo, or sperm cryopreservation prior to planned chemotherapy.[1-4] Multiple-embryo transfer is associated with an increased risk for multiple-gestation pregnancies and pregnancy complications, including cesarean birth, preeclampsia, premature delivery, and low-birth-weight infants.[5, 6] Additionally, analysis of a US database found a significant adverse effect on intrauterine growth for live singleton and twin births resulting from transfer of multiple embryos.[7] Guidelines on the number of embryos to transfer have been developed by professional societies in order to optimize healthy live births and minimize multiple-gestation pregnancies.[8-10] Assisted reproductive technology registries from 36 European countries for 2008 show an overall distribution of the transfer of 1, 2, 3, and 4 or more embryos as 22.4%, 53.2%, 22.3%, and 2.1%, respectively, resulting in proportions of singleton, twin, and triplet deliveries of 78.3%, 20.7%, and 1.0%, respectively.[11] A systematic review and meta-analysis of randomized controlled trials concluded that increasing the number of single-embryo transfer attempts to 3 cycles using fresh or frozen embryos in women younger than 36 years results in a cumulative live birth rate similar to double-embryo transfer and reduces the likelihood of multiple births by 94%.[12] A meta-

analysis of individual patient data from randomized trials reported that elective single-embryo transfer resulted in a lower pregnancy rate than double-embryo transfer in a fresh in vitro fertilization cycle; however, the difference was almost completely overcome by an additional frozen single-embryo transfer cycle. Additionally, the rate of multiple-gestation pregnancy and risk of preterm birth and delivery of a low-birth-weight infant were decreased with single-embryo transfer.[13] A systematic review and meta-analysis reported that elective single-embryo transfer is associated with decreased risk of preterm birth and low birth weight as compared with double-embryo transfer, but with higher risk of preterm birth as compared with spontaneously conceived singleton infants.[14] A multicenter randomized controlled trial of 1650 women with infertility found that frozen single blastocyst transfer was associated with an improved singleton live birth rate compared with fresh single blastocyst transfer (50% vs 40%, respectively). However, frozen single blastocyst transfer was also associated with a higher risk of preeclampsia (3.1% vs 1.0%, respectively) which the authors advise warrants additional evaluation.[15] A national registry study of the outcomes by number of embryos transferred (124,148 IVF cycles, 32,732 cycles with complete outcomes data available) reported that the odds of live birth were similar regardless of whether 1, 2, or 3 embryos were transferred; however, all adverse perinatal outcomes (multiple births, prematurity, small for gestational age) occurred more frequently when 3 or more embryos were transferred. The odds of live birth were higher with double-embryo transfer in all age groups; however, the association was stronger in women older than 40 years. Multiple birth risk increased with double-embryo transfer in all age groups, but was substantially lower in women age 40 years and older. The authors concluded that the findings supported restricting embryo transfer to fewer than 3.[16] A practice guideline recommends that women age 35 to 40 years be considered for elective single-embryo transfer if they have top-quality blastocyst-stage embryos available for transfer.[17] For women age 40 to 42 years, another practice guideline recommends double-embryo transfer.[2]

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