Anthem

Clinical UM Guideline

Subject: Preimplantation Embryo Biopsy
Guideline #: CG-MED-88
Status: Revised

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Description

Preimplantation embryo biopsy is performed to allow for genetic testing (PGT), which encompasses a variety of adjunctive techniques to assisted reproductive procedures, in which embryonic DNA is sampled and genetically analyzed, thus permitting deselection of embryos harboring a genetic defect prior to implantation of the embryo into the uterus. These procedures may be performed as part of assisted reproductive technology (ART).

Note: This document addresses preimplantation embryo biopsy *only*. This document does not address genetic testing, including for aneuploidies (PGT-A), monogenic disorders (PGT-M), or structural rearrangements (PGT-SR). For criteria related to genetic testing, please refer to the applicable guidelines used by the plan.

Note: The use of in vitro fertilization (IVF) services is subject to separate Benefit Determination, independent of this position statement. Not all benefit contracts or certificates include benefits for IVF services, including preimplantation embryo biopsy. Preimplantation embryo biopsy is only covered when IVF services are covered benefits. Benefit language supersedes this document.

Clinical Indications

Medically Necessary:

Preimplantation embryo biopsy is considered **medically necessary** when conducted for preimplantation genetic testing that meets the applicable guidelines used by the plan.

Not Medically Necessary:

Preimplantation embryo biopsy is considered **not medically necessary** when the criteria above have not been met.

Coding

The following codes for treatments and procedures applicable to this guideline are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services may be Medically Necessary when criteria are met:

CPT	
89290	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for preimplantation genetic diagnosis); less than or equal to 5 embryos
89291	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for preimplantation genetic diagnosis); greater than 5 embryos

ICD-10 Diagnosis	
	All diagnoses

When services are Not Medically Necessary:
For the procedure codes listed above when criteria are not met.

Discussion/General Information

Embryo biopsy for PGT is conducted to evaluate DNA from embryos in order to significantly reduce the risk of inherited diseases and chromosomal abnormalities (for example, aneuploidy and structural rearrangements). PGT starts with IVF followed by embryo biopsy and preparation of DNA from the embryonic cells for testing. Subsequently, the healthiest embryos selected based on the results of genetic testing are transferred into the uterus to continue development.

The embryo biopsy procedure required for PGT involves two steps: the opening of the zona pellucida (the membrane covering the embryo) and retrieval of the cells for genetic testing. Biopsy can be performed at day 3 of cleavage-stage embryo development when the embryo is at the six- to the eight-cell stage, with either one or two cells (blastomeres) being removed for analysis (Vlajkovic, 2022). However, the most common method of embryo biopsy entails collecting cells at the blastocyst stage of development. The blastocyst stage is reached at 5-6 days following fertilization and usually contains more than 100 cells. During the biopsy, approximately 5-10 cells are removed from the trophectoderm layer, the outer portion of the blastocyst that gives rise to the placenta, without disrupting the inner cell mass that is destined to become the fetus (American College of Obstetrics and Gynecology, 2020). Compared with other methods for obtaining DNA for PGT, including sampling polar bodies or a blastomere from a cleavage-stage embryo, blastocyst biopsy is the least disruptive to subsequent embryo development while providing the most DNA for testing (Scott, 2013). Addressing the potential for embryo damage caused by biopsy, the American Society for Reproductive Medicine (2018) states that:

> There are few data on embryo biopsy techniques used in PGT-A; however, it is generally accepted that trophectoderm biopsy has less impact on embryo viability than cleavage-stage biopsy. This is because even though more cells are removed during trophectoderm biopsy, it represents a smaller percentage of embryo mass and, by definition, trophectoderm biopsy removes only trophectoderm cells and not cells that have any fetal fate. Conversely, cleavage-stage biopsy occurs at a time when cell lineage has not yet been established and the cell removed could potentially impact viability of the embryo and the fate of the fetus.

Noninvasive and/or minimally invasive PGT (niPGT) is an emerging technique involving collection of cell-free DNA released from

preimplantation embryos, including fluids in the blastocysts, spent culture medium, or both. This technique does not involve embryo biopsy and thus has the potential to reduce embryo damage. However, lower detection rates and DNA contamination from maternal cells may be associated with this technique. Prospective, large-scale studies are needed to determine the accuracy and detection value of niPGT (Huang, 2023).

Definitions

Aneuploidy: A condition where there are either fewer or more than the normal number of chromosomes present in cells of a person's body.

Embryo biopsy: A procedure conducted during an assisted reproduction process where, following the fertilization process, cells are removed from the developing embryo and used for genetic testing.

In vitro fertilization (IVF): A type of assisted reproductive procedure where an egg is fertilized outside a woman's body and then implanted into the womb.

Oocyte: An egg before maturation.

Preimplantation genetic testing (PGT): A technique in which embryonic DNA is sampled via embryo biopsy and genetically analyzed to identify abnormal embryos and to select only genetically normal embryos for implantation.

Zona pellucida: A thick specialized membrane that surrounds mammalian oocytes.

References

Peer Reviewed Publications:

1. Huang B, Luo X, Wu R, et al. Evaluation of non-invasive gene detection in preimplantation embryos: a systematic review and meta-analysis. J Assist Reprod Genet. 2023; 40(6):1243-1253.
2. Scott RT, Jr., Upham KM, Forman EJ, et al. Cleavage-stage biopsy significantly impairs human embryonic implantation potential while blastocyst biopsy does not: a randomized and paired clinical trial. Fertil Steril. 2013; 100(3):624-630.
3. Vlajkovic T, Grigore M, van Eekelen R, Puscasiu L. Day 5 versus day 3 embryo biopsy for preimplantation genetic testing for monogenic/single gene defects. Cochrane Database Syst Rev. 2022; 11(11):CD013233.

Government Agency, Medical Society, and Other Authoritative Publications:

1. American College of Obstetrics and Gynecology. Preimplantation Genetic Testing: ACOG Committee Opinion, Number 799. Obstet Gynecol. 2020; 135(3):e133-137.
2. Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. The use of preimplantation genetic testing for aneuploidy (PGT-A): a committee opinion. Fertl Steril. 2018; 109:429-436.

History

Status	Date	Action
Revised	02/15/2024	Medical Policy & Technology Assessment Committee (MPTAC) review. Revised title to Preimplantation Embryo Biopsy. Revised Clinical Indications to address preimplantation embryo biopsy only. Removed genetic testing-related content (other criteria is available). Revised Description, Discussion/General Information, Definitions and References sections. Revised Coding section, removed 0254U, 0396U no longer applicable, other criteria is available.
Revised	08/10/2023	MPTAC review. Revised terminology to replace PGS with PGT-A, and PGD with PGT-M or PGT-SR. Reformatted MN criteria. Created new MN criteria for PGT-SR. Revised genetic counseling requirements. Updated Description, Discussion/General Information, Definitions and References sections. Updated Coding section to add CPT (PLA) codes 0254U, 0396U.
Revised	02/16/2023	MPTAC review. Revised title to Preimplantation Embryo Biopsy and Genetic Testing. Updated Description, Discussion/General Information, Definitions and References sections.
Reviewed	02/17/2022	MPTAC review. Updated Discussion/General Information and References sections.
Revised	02/11/2021	MPTAC review. Clarified language in the Clinical Indications section regarding preimplantation genetic testing/screening for fetal aneuploidy (PGT-A). Updated Description, Background and References sections. Reformatted Coding section.
Revised	02/20/2020	MPTAC review. Changed document category and number from CG-GENE-06 to CG-MED-88. Added new MN and NMN statements addressing preimplantation embryo biopsy. Updated Description, Background, Definitions, and References sections.
New	03/21/2019	MPTAC review. Initial document development. Moved content of GENE.00002 Preimplantation Genetic Diagnosis Testing to new clinical utilization management guideline document with the same title.

guideline for provider education and/or to review the medical necessity of services for any provider who has been notified that his/her/its claims will be reviewed for medical necessity due to billing practices or claims that are not consistent with other providers, in terms of frequency or in some other manner.