

BSC_CON_2.03	Genetic Testing: Preimplantation Genetic Testing		
Original Policy Date:	January 1, 2023	Effective Date:	January 1, 2023
Section:	4.0 OB/Gyn/Reproduction	Page:	Page 1 of 9

Example Test Table

Below is a list of higher volume tests and the associated laboratories for each coverage criteria section. This list is not all inclusive.

Policy Statement Sections	Example Tests (Labs)	Common CPT Codes
Preimplantation Genetic Testing for Aneuploidy (PGT-A)	Spectrum PGT-A (Natera)	89290, 89291, 81479
	Preimplantation Genetic Testing for Chromosomal Aneuploidy (Invitae)	
	SMART PGT-A (Preimplantation Genetic Testing - Aneuploidy) (Igenomix)	0254U
Preimplantation Genetic Testing for Monogenic Disorders (PGT-M)	Spectrum PGT-M (Natera)	89290, 89291, 81479
	PGT-M (Cooper Genomics)	81403
Preimplantation Genetic Testing for Structural Rearrangements (PGT-SR)	Preimplantation Genetic Testing for Structural Chromosomal Rearrangements/Translocations (Invitae)	89290, 89291, 81479, 81403, 81228, 88291
	Spectrum PGT-SR (Natera)	81479

Policy Statement

Preimplantation Genetic Testing for Aneuploidy (PGT-A)

- I. Preimplantation genetic testing for aneuploidy (PGT-A) (89290, 89291, 0254U, 81479) is considered **investigational**.

Preimplantation Genetic Testing for Monogenic Disorders (PGT-M)

- II. Preimplantation genetic testing for monogenic disorders (PGT-M) (89290, 89291, 81479, 81403) may be considered **medically necessary** when:
 - A. The embryo is at an elevated risk of a genetic disorder due to one of the following:
 - 1. Both biological parents are known carriers for the same autosomal recessive disorder, **OR**
 - 2. One biological parent is a known carrier of an autosomal dominant disorder, **OR**
 - 3. One biological parent is a known carrier of an X-linked recessive disorder.
- III. Preimplantation genetic testing for monogenic disorders (PGT-M) (89290, 89291, 81479, 81403) is considered **investigational** for all other indications.

Preimplantation Genetic Testing for Structural Rearrangements (PGT-SR)

- IV. Preimplantation genetic testing for structural rearrangements (PGT-SR) (81228, 88291, 89290, 89291, 81479, 81403) may be considered **medically necessary** when:
 - A. The embryo is at an elevated risk of a genetic disorder because one biological parent has a chromosomal rearrangement.
- V. Preimplantation genetic testing for structural rearrangements (PGT-SR) (81228, 88291, 89290, 89291, 81479, 81403) is considered **investigational** for all other indications.

Preimplantation Genetic Diagnosis and Screening

- VI. Preimplantation genetic *diagnosis* (PGD) as an adjunct to IVF is considered **investigational** in individuals or couples who are undergoing IVF in all situations other than those specified above.
- VII. Preimplantation genetic *screening* (PGS) as an adjunct to IVF is considered **investigational** in individuals or couples who are undergoing IVF in all situations.

NOTE: Refer to [Appendix A](#) to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Notes and Definitions

1. Close relatives include first, second, and third degree blood relatives on the same side of the family:
 - a. First-degree relatives are parents, siblings, and children
 - b. Second-degree relatives are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings
 - c. Third-degree relatives are great grandparents, great aunts, great uncles, great grandchildren, and first cousins
2. Preimplantation genetic testing for monogenic disorders (PGT-M) and Preimplantation genetic testing for structural rearrangements (PGT-SR) are used to detect a specific single-gene inherited disorder or chromosome rearrangement in conjunction with in vitro fertilization (IVF)
3. Preimplantation genetic testing for aneuploidy (PGT-A) is used to screen for chromosomal aneuploidy in conjunction with IVF for couples.

Clinical Considerations

Genetic counseling is highly encouraged for patients considering and undergoing in vitro fertilization. Genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods, such as a genetic counselor, medical geneticist, or advanced practice practitioner specializing in genetics.

All patients who undergo PGT-M or PGT-SR should be offered diagnostic testing via chorionic villus sampling (CVS) or amniocentesis for confirmation of results.

All patients who undergo PGT-A should be offered traditional diagnostic testing or screening for aneuploidy in accordance with recommendations for all pregnant patients.

Description

Preimplantation genetic testing involves analysis of biopsied cells from an embryo as a part of an assisted reproductive procedure. Preimplantation genetic testing for monogenic disorders (PGT-M) and preimplantation genetic testing for structural rearrangements (PGT-SR) are used to detect a specific inherited disorder in conjunction with in vitro fertilization (IVF) and aims to prevent the birth of affected children to couples at an increased risk of transmitting either a gene mutation(s) or an unbalanced structural chromosomal rearrangement that can be typically targeted in this context. Preimplantation genetic testing for aneuploidy (PGT-A) is used to screen for potential chromosomal or subchromosomal abnormalities (e.g., chromosomal aneuploidy) in conjunction with IVF for couples; in this case testing is untargeted.

Related Policies

This policy document provides coverage criteria for preimplantation genetic testing. Please refer to:

- **Genetic Testing: Prenatal and Preconception Carrier Screening** for coverage criteria related to carrier screening. *(To be published)*
- **Genetic Testing: Prenatal Diagnosis (via amniocentesis, CVS, or PUBS) and Pregnancy Loss** for coverage related to diagnostic genetic testing during pregnancy or for a pregnancy loss. *(To be published)*
- **Genetic Testing: Noninvasive Prenatal Screening (NIPS)** for coverage criteria related to prenatal cell-free DNA screening tests. *(To be published)*
- **Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay** for coverage criteria related to diagnostic genetic testing in the postnatal period. *(To be published)*
- **Genetic Testing: General Approach to Genetic Testing** for coverage criteria related to preimplantation genetic testing that is not specifically discussed in this or another non-general policy. *(To be published)*

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. 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.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Rationale

Preimplantation Genetic Testing for Aneuploidy (PGT-A)

American Society of Reproductive Medicine

The American Society for Reproductive Medicine issued an opinion on the use of preimplantation genetic testing (PGS) for aneuploidy (2018) which concluded, "Large, prospective, well-controlled studies evaluating the combination of multiple approaches (genomics, time-lapse imaging, transcriptomics, proteomics, metabolomics, etc.) for enhanced embryo selection applicable in a more inclusive IVF population are needed to determine not only the effectiveness, but also the safety and potential risks of these technologies. PGT-A will likely be part of a future multidimensional approach to embryo screening and selection. At present, however, there is insufficient evidence to recommend the routine use of blastocyst biopsy with aneuploidy testing in all infertile patients."

This position was reaffirmed in a 2020 committee opinion regarding clinical management of mosaic results from preimplantation genetic testing for aneuploidy of blastocysts, stating, "It should be recognized that this document does not endorse nor does it suggest that PGT-A is appropriate for all cases of IVF."

American College of Obstetricians and Gynecologists (ACOG)

The American College of Obstetricians and Gynecologists issued Committee Opinion No. 799 (2020) regarding Preimplantation Genetic Testing. The recommendations include the following:

"The main purpose of preimplantation genetic testing-aneuploidy (known as PGT-A) is to screen embryos for whole chromosome abnormalities. Traditional diagnostic testing or screening for

aneuploidy should be offered to all patients who have had preimplantation genetic testing-aneuploidy, in accordance with recommendations for all pregnant patients."

The American College of Obstetricians and Gynecologists (2015, reaffirmed 2017) issued an opinion that recommends "[p]atients with established causative mutations for a genetic condition" who are undergoing in vitro fertilization and desire prenatal genetic testing should be offered the testing, either preimplantation or once pregnancy is established.

Preimplantation Genetic Testing for Monogenic Disorders (PGT-M)

American Society for Reproductive Medicine

The American Society for Reproductive Medicine published an opinion on the use of preimplantation genetic diagnosis (PGD) for serious adult-onset conditions (2013). The statement includes the following:

- "Preimplantation genetic diagnosis (PGD) for adult-onset conditions is ethically justifiable when the conditions are serious and when there are no known interventions for the conditions or the available interventions are either inadequately effective or significantly burdensome."
- "For conditions that are less serious or of lower penetrance, PGD for adult[-]onset conditions is ethically acceptable as a matter of reproductive liberty. It should be discouraged, however, if the risks of PGD are found to be more than merely speculative."

The opinion also stated that physicians and patients should be aware that much remains unknown about the long-term effects of embryo biopsy on the developing fetus and that experienced genetic counselors should be involved in the decision process.

American College of Obstetricians and Gynecologists (ACOG)

The American College of Obstetricians and Gynecologists issued Committee Opinion No. 799 (2020) regarding Preimplantation Genetic Testing. The recommendations include the following:

"Preimplantation genetic testing comprises a group of genetic assays used to evaluate embryos before transfer to the uterus. Preimplantation genetic testing-monogenic (known as PGT-M) is targeted to single gene disorders. Preimplantation genetic testing-monogenic uses only a few cells from the early embryo, usually at the blastocyst stage, and misdiagnosis is possible but rare with modern techniques. Confirmation of preimplantation genetic testing-monogenic results with chorionic villus sampling (CVS) or amniocentesis should be offered."

The American College of Obstetricians and Gynecologists (2015, reaffirmed 2017) issued an opinion that recommends "[p]atients with established causative mutations for a genetic condition" who are undergoing in vitro fertilization and desire prenatal genetic testing should be offered the testing, either preimplantation or once pregnancy is established.

Preimplantation Genetic Testing for Structural Rearrangements (PGT-SR)

American College of Obstetricians and Gynecologists (ACOG)

The American College of Obstetricians and Gynecologists issued Committee Opinion No. 799 (2020) regarding Preimplantation Genetic Testing. The recommendations include the following: "To detect structural chromosomal abnormalities such as translocations, preimplantation genetic testing-structural rearrangements (known as PGT-SR) is used. Confirmation of preimplantation genetic testing-structural rearrangements results with CVS or amniocentesis should be offered."

References

1. Ethics Committee of American Society for Reproductive Medicine. Use of preimplantation genetic diagnosis for serious adult onset conditions: a committee opinion. *Fertil Steril*. 2013;100(1):54-57. doi:10.1016/j.fertnstert.2013.02.043

2. Preimplantation Genetic Testing: ACOG Committee Opinion, Number 799. *Obstet Gynecol.* 2020;135(3):e133-e137. doi:10.1097/AOG.0000000000003714
3. Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology. Electronic address: ASRM@asrm.org; 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. *Fertil Steril.* 2018;109(3):429-436. doi:10.1016/j.fertnstert.2018.01.002
4. Practice Committee and Genetic Counseling Professional Group (GCPG) of the American Society for Reproductive Medicine. Electronic address: asrm@asrm.org. Clinical management of mosaic results from preimplantation genetic testing for aneuploidy (PGT-A) of blastocysts: a committee opinion. *Fertil Steril.* 2020;114(2):246-254. doi:10.1016/j.fertnstert.2020.05.014

Documentation for Clinical Review

Please provide the following documentation:

- History and physical and/or consultation notes including:
 - Reason for performing test
 - Signs/symptoms/test results related to reason for genetic testing
 - Family history if applicable
 - How test result will impact clinical decision making
 - Lab results documenting one/both partners carrier status or genetic disorder
 - Physician order for genetic test
 - Name and description of genetic test
 - CPT codes billed for the particular genetic test
 - Name of the test being requested or the Concert Genetics GTU identifier
- The Concert Genetics GTU can be found at <https://app.concertgenetics.com>

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	0254U	Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using embryonic DNA genomic sequence analysis for aneuploidy, and a mitochondrial DNA score in euploid embryos, results reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploidy, per embryo tested
	81228	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number variants, comparative genomic hybridization [CGH] microarray analysis
	81403	MOLECULAR PATHOLOGY PROCEDURE LEVEL 4
	81479	Unlisted molecular pathology procedure
	88291	Cytogenetics and molecular cytogenetics, interpretation and report

Type	Code	Description
	89290	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); less than or equal to 5 embryos
	89291	Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); greater than 5 embryos
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
01/01/2023	New policy.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue

Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE <u>Red font: Verbiage removed</u>	AFTER <u>Blue font: Verbiage Changes/Additions</u>
<p>Preimplantation Genetic Testing 4.02.05</p> <p>Policy Statement:</p> <ol style="list-style-type: none"> I. Preimplantation genetic <i>diagnosis</i> (PGD) may be considered medically necessary as an adjunct to in vitro fertilization (IVF) in couples not known to be infertile who meet one of the criteria listed below: <ol style="list-style-type: none"> A. For evaluation of an embryo at an identified elevated risk of a genetic disorder such as when: <ol style="list-style-type: none"> 1. Both partners are known carriers of a single-gene autosomal recessive disorder 2. One partner is a known carrier of a single-gene autosomal recessive disorder, and the partners have an offspring who has been diagnosed with that recessive disorder 3. One partner is a known carrier of a single-gene autosomal dominant disorder 4. One partner is a known carrier of a single X-linked disorder B. For evaluation of an embryo at an identified elevated risk of structural chromosomal abnormality such as for a: <ol style="list-style-type: none"> 1. Parent with balanced or unbalanced chromosomal translocation. 	<p>Genetic Testing: Preimplantation Genetic Testing BSC_CON_2.03</p> <p>Policy Statement:</p> <p>Preimplantation Genetic Testing for Aneuploidy (PGT-A)</p> <ol style="list-style-type: none"> I. Preimplantation genetic testing for aneuploidy (PGT-A) (89290, 89291, 0254U, 81479) is considered investigational. <p>Preimplantation Genetic Testing for Monogenic Disorders (PGT-M)</p> <ol style="list-style-type: none"> II. Preimplantation genetic testing for monogenic disorders (PGT-M) (89290, 89291, 81479, 81403) may be considered medically necessary when: <ol style="list-style-type: none"> A. The embryo is at an elevated risk of a genetic disorder due to one of the following: <ol style="list-style-type: none"> 1. Both biological parents are known carriers for the same autosomal recessive disorder, OR 2. One biological parent is a known carrier of an autosomal dominant disorder, OR 3. One biological parent is a known carrier of an X-linked recessive disorder. III. Preimplantation genetic testing for monogenic disorders (PGT-M) (89290, 89291, 81479, 81403) is considered investigational for all other indications. <p>Preimplantation Genetic Testing for Structural Rearrangements (PGT-SR)</p> <ol style="list-style-type: none"> IV. Preimplantation genetic testing for structural rearrangements (PGT-SR) (81228, 88291, 89290, 89291, 81479, 81403) may be considered medically necessary when: <ol style="list-style-type: none"> A. The embryo is at an elevated risk of a genetic disorder because one biological parent has a chromosomal rearrangement.

POLICY STATEMENT

BEFORE <u>Red font: Verbiage removed</u>	AFTER <u>Blue font: Verbiage Changes/Additions</u>
<p>II. Preimplantation genetic <i>diagnosis</i> (PGD) as an adjunct to IVF is considered not medically necessary in individuals or couples who are undergoing IVF in all situations other than those specified above.</p> <p>III. Preimplantation genetic <i>screening</i> (PGS) as an adjunct to IVF is considered not medically necessary in individuals or couples who are undergoing IVF in all situations.</p>	<p>V. Preimplantation genetic testing for structural rearrangements (PGT-SR) (81228, 88291, 89290, 89291, 81479, 81403) is considered investigational for all other indications.</p> <p>Preimplantation Genetic Diagnosis and Screening</p> <p>VI. Preimplantation genetic <i>diagnosis</i> (PGD) as an adjunct to IVF is considered investigational in individuals or couples who are undergoing IVF in all situations other than those specified above.</p> <p>VII. Preimplantation genetic <i>screening</i> (PGS) as an adjunct to IVF is considered investigational in individuals or couples who are undergoing IVF in all situations.</p>