Medical Policy
Preimplantation Genetic Testing

Table of Contents
- Policy: Commercial
- Policy: Medicare
- Authorization Information
- Coding Information
- Description
- Policy History
- Information Pertaining to All Policies
- References
- Endnotes

Policy Number: 088
BCBSA Reference Number: 4.02.05

Related Policies
- Reproductive Techniques, #475

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

Preimplantation genetic diagnosis (PGD) may be MEDICALLY NECESSARY as an adjunct to in vitro fertilization (IVF) in couples not known to be infertile who meet one of the following criteria subject to careful consideration of the technical and ethical issues involved:
- For evaluation of an embryo at an identified elevated risk of a genetic disorder, such as when:
  - Both partners are known carriers of a single gene autosomal recessive disorder,
  - One partner is a known carrier of a single gene autosomal recessive disorder and the partners have one offspring that has been diagnosed with that recessive disorder,
  - One partner is a known carrier of a single gene autosomal dominant disorder, or
  - One partner is a known carrier of a single X-linked disorder.
- For evaluation of an embryo at an identified elevated risk of structural chromosomal abnormality, such as for a:
  - Parent with balanced or unbalanced chromosomal translocation.

Preimplantation genetic diagnosis (PGD) as an adjunct to IVF is INVESTIGATIONAL in patients/couples who are undergoing IVF in all situations other than those specified above.

Preimplantation genetic screening (PGS) as an adjunct to IVF is INVESTIGATIONAL in patients/couples who are undergoing IVF in all situations.
Preimplantation genetic testing for all other indications, including a parent with a documented history of aneuploidy in a previous pregnancy, is INVESTIGATIONAL.1

Prior Authorization Information
Commercial Members: Managed Care (HMO and POS)
Prior authorization is required.
Commercial Members: PPO, and Indemnity
Prior authorization is required.

Medicare Members: HMO BlueSM
Prior authorization is required.

Medicare Members: PPO BlueSM
Prior authorization is required.

CPT Codes / HCPCS Codes / ICD-9 Codes
The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>89290</td>
<td>Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); less than or equal to 5 embryos</td>
</tr>
<tr>
<td>89291</td>
<td>Biopsy, oocyte polar body or embryo blastomere, microtechnique (for pre-implantation genetic diagnosis); greater than 5 embryos</td>
</tr>
</tbody>
</table>

Description
Preimplantation genetic testing (PGT) involves analysis of biopsied cells as part of an assisted reproductive procedure. It is generally considered to be divided into two categories:

- Preimplantation genetic diagnosis (PGD) is used to detect a specific inherited disorder and aims to prevent the birth of affected children in couples at high risk of transmitting a disorder.
- Preimplantation genetic screening (PGS) uses similar techniques to screen for potential genetic abnormalities in conjunction with in vitro fertilization for couples without a specific known inherited disorder.

Preimplantation genetic testing (PGT) describes a variety of adjuncts to an assisted reproductive procedure in which either maternal or 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. The ability to identify preimplantation embryos with genetic defects before the initiation of pregnancy provides an attractive alternative to amniocentesis or chorionic villus sampling (CVS), with selective pregnancy termination of affected fetuses.

Two different sources of genetic material may be sampled in PGT; either the first or second polar body of the oocyte may be sampled which focuses on maternal chromosomal abnormalities or the preimplantation embryo may be biopsied to detect genetic abnormalities arising from the maternal or paternal genetic material.

The biopsied material can be analyzed in a variety of ways. Polymerase chain reaction (PCR) or other amplification techniques can be used to amplify the harvested DNA with subsequent analysis for single genetic defects. This technique is most commonly used when the embryo is at risk for a specific genetic disorders such as Tay Sachs disease or cystic fibrosis. Fluorescent in situ hybridization (FISH) is a technique that allows direct visualization of specific (but not all) chromosomes to determine the number or absence of chromosomes. This technique is most commonly used to screen for aneuploidy, gender determination or to identify chromosomal translocations. FISH cannot be used to diagnose single genetic defect disorders. However, molecular techniques can be applied with FISH (such as microdeletions and duplications) and thus, single-gene defects can be recognized with this technique.
Another approach that is becoming more common is array comparative genome hybridization (CGH) testing at either the 8-cell or more often, the blastocyst stage. Unlike FISH analysis, this allows for 24 chromosome aneuploidy screening, as well as more detailed screening for unbalanced translocations and inversions and other types of abnormal gains and losses of chromosomal material.

Three general categories of embryos have undergone PGT:

1. **Embryos at risk for a specific inherited single genetic defect**
   Inherited single-gene defects fall into 3 general categories: autosomal recessive, autosomal dominant, and X-linked. When either the mother or father is a known carrier of a genetic defect, embryos can undergo PGD to deselect embryos harboring the defective gene. Gender selection of a female embryo is another strategy when the mother is a known carrier of an X-linked disorder for which there is not yet a specific molecular diagnosis. The most common example is female carriers of fragile X syndrome. In this scenario, PGD is used to deselect male embryos, half of which would be affected. PGD could also be used to deselect affected male embryos. While there is a growing list of single genetic defects for which molecular diagnosis is possible, the most common indications include cystic fibrosis, beta thalassemia, muscular dystrophy, Huntington's disease, hemophilia, and fragile X disease. It should be noted that when PGD is used to deselect affected embryos, the treated couple is not technically infertile but are undergoing an assisted reproductive procedure for the sole purpose of PGD. In this setting, PGD may be considered an alternative to selective termination of an established pregnancy after diagnosis by amniocentesis or chorionic villus sampling.

2. **Embryos at a higher risk of translocations**
   Balanced translocations occur in 0.2% of the neonatal population but at a higher rate in infertile couples or in those with recurrent spontaneous abortions. PGD can be used to deselect those embryos carrying the translocations, thus leading to an increase in fecundity or a decrease in the rate of spontaneous abortion.

3. **Identification of aneuploid embryos**
   Implantation failure of fertilized embryos is a common cause for failure of assisted reproductive procedures; aneuploidy of embryos is thought to contribute to implantation failure and may also be the cause of recurrent spontaneous abortion. The prevalence of aneuploid oocytes increases in older women. These age-related aneuploidies are mainly due to nondisjunction of chromosomes during maternal meiosis. Therefore, PGS of the extruded polar bodies from the oocyte has been explored as a technique to deselect aneuploid oocytes in older women. The FISH technique is most commonly used to detect aneuploidy.

**Summary**
Preimplantation genetic testing has been shown to be technically feasible in detecting single gene defects, structural chromosomal abnormalities, and aneuploid embryos using a variety of biopsy and molecular diagnostic techniques. Ultimately, the choice is one of the risks (both medical and psychological) of undergoing IVF with PGD, compared to the option of normal fertilization and pregnancy with the possibility of a subsequent elective abortion.

PGD is considered medically necessary, as noted in the policy statements, when the evaluation is focused on a known disease or disorder, and the decision to undergo PGD is made upon careful consideration of the risks and benefits. There is insufficient evidence that preimplantation genetic screening improves ongoing pregnancy and live birth rates; thus, preimplantation genetic screening as an adjunct to in vitro fertilization is considered investigational.

**Policy History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>9/2014</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
</tbody>
</table>
| 1/2014 | BCBSA National medical policy review.  
Information Pertaining to All Blue Cross Blue Shield Medical Policies
Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References


Endnotes

1 Based on ASRM guidelines