KAISER PERMANENTE® Mid-Atlantic States	**Preimplantation Genetic Testing (PGT) Medical Coverage Policy**

UTILIZATION * ALERT*

- Prior to use of this MCP for evaluation of medical necessity, benefit coverage MUST be verified in the member's EOC or benefit document.
- All coverage is subject to the terms and conditions of the member's benefit plan; coverage varies widely for diagnosis and treatment of infertility, and in exclusions and limitations of procedures.
- PGD is considered a procedure separate from infertility procedures; testing when criteria for coverage are met is covered under the laboratory services benefit.
- Medicare currently does not have a National Coverage Determination (NCD) for Preimplantation Genetic Testing.
- In addition, Local coverage determinations (LCD)/Local Coverage Articles (LCA) do not exist at this time.
- If, after searching the Medicare Coverage Database, no NCD/LCD/LCA is found, please use this KP-MAS Medical Coverage Policy for coverage guidelines for Medicare members.

I. Procedure: Preimplantation Genetic Testing (PGT)

II. Diagnosis: Embryonic risk for genetic disorders

III. Specialties: Genetics and Reproductive Endocrinology

IV. Indications for Coverage

A. Preimplantation Genetic Testing (PGT) for Monogenic/single gene defects (PGT-M) or inherited structural chromosome rearrangements (PGT-SR) is covered for detection of a genetic disorder in an embryo as follows:

1. For autosomal recessive conditions when both parents are known carriers, or one parent is a known carrier and the couple has previously produced offspring affected by that disorder **and** when the disorder is associated with possible severe disability or lethal history; ***or***

2. For autosomal dominant disorders, when at least one parent is diagnosed, and when the disorder is associated with possible severe disability or lethal history

3. For X-linked disorders, when at least one parent is diagnosed, when the disorder is associated with possible severe disability or lethal history

4. Balanced or unbalanced chromosomal translocations of one of the parents

B. PGT-M and PGT-SR treatment and coverage is not limited solely to women or couples diagnosed with infertility requiring advanced reproductive technologies. PGT-M is medically necessary to diagnose specific detectable genetic mutations (Cystic Fibrosis, fragile X) where there is a valid genetic test based on peer-reviewed literature and/or MCG care guidelines.

C. PGT-M and PGT-SR treatment requires in vitro fertilization (IVF) as a secondary process. The IVF services, including oocyte/follicle retrieval, and embryo transfer, are covered when the patient meets the definition of infertility and has the IVF benefit.

D. Assisted hatching is only covered when IVF is covered. Assisted hatching is not covered when only PGT-M or PGT-SR are covered;

E. ICSI (Intracytoplasmic Sperm Injection) is only covered for PGT-M for single gene disorders where PCR testing will be needed. In all other cases, ICSI is only covered when IVF is covered, and medical necessity is met.

V. Exclusions/Limitations

A. KPMAS considers preimplantation genetic testing for aneuploidy (PGT-A) i.e., screening embryos for chromosomal abnormalities in the absence of specific inherited genetic conditions identified in either parent to be experimental or investigational, including the following:
1. Preimplantation genetic screening and comprehensive chromosome screening of polar bodies and blastocysts to enhance delivery rates in advanced reproductive technologies;
2. Aneuploidy screening (AS) in the setting PGT-A for purposes of optimizing IVF outcomes in women with advanced maternal age, history of failed IVF cycles, or recurrent miscarriages, in the absence of inherited genetic abnormalities.

B. Preimplantation genetic diagnosis for fetal chromosomal abnormalities is currently not as accurate as cytogenetic analysis performed on prenatal diagnostic specimens obtained by chorionic villus sampling and amniocentesis. Therefore, PGT-A is considered experimental and investigational for detecting fetal chromosomal abnormalities.
C. PGT for nonmedical gender selection and/or nonmedical traits
D. PGT for multifactorial inheritance disorders
E. PGT for hereditary mutations which manifest in adulthood (e.g., BRCA testing)
F. PGT for screening of conditions with incomplete penetrance or significant variability of expression (e.g., Alzheimer's disease, cancer predisposition)
G. Screening for polygenic risk (PGT-P)

References

1. Collins FS. A Brief Primer on Genetic Testing - World Economic Forum National Human Genome Research Institute, January 24, 2003. genome.gov. Accessed 3/16/2015.
2. Cooper AR. Preimplantation genetic testing: indications and controversies. - Clin Lab Med. Sep 2010; 30(3): 519-31.
3. Essawi ML, Al-Attribi GM, Gaber KR, El-Harouni AA. Molecular prenatal diagnosis of autosomal recessive childhood spinal muscular atrophies (SMAs). Gene 2012;509(1):120-3.
4. Genetic counselling. GeneReviews illustrated glossary [Internet] University of Washington. Accessed at: http://www.ncbi.nlm.nih.gov/books/NBK5191/#IX-G. Updated 2014. Accessed 4/9/2016.
5. Harper JC. The ESHRE PGD Consortium: 10 years of data collection. - Hum Reprod Update – May 2012; 18(3): 234-47.
6. Harton GL Best practice guidelines for polar body and embryo biopsy for preimplantation genetic diagnosis/screening (PGD/PGS). ESHRE PGD Consortium/Embryology Special Interest Group. Hum Reprod Jan -2011; 26(1): 41-6.
7. Iwarsson E, Malmgren H, Blennow E. Preimplantation genetic diagnosis: twenty years of practice. Semin Fetal Neonatal Med Apr 2011; 16(2): 74-80.
8. Kaiser Permanente Interregional New Technologies Committee, "Genetic Testing." https://clm.kp.org/wps/portal/cl/MAS/search_iframe?query=INTC . Accessed Mar 16, 2015.
9. Kroese AC, de Lange NM, Collins J, Evers JL. Surgery, or embolization for varicoceles in subfertile men. Cochrane Database of Systematic Reviews 2012, Issue 10. Art. No.: CD000479.
10. Medicare Coverage Database, "Genomic Testing," Defer to MEDAC advisory. Accessed 7/29/2016.
11. Meiri E, Mueller WC, Rosenwald S et al. A second-generation microRNA-based assay for diagnosing tumor tissue origin. Oncologist. 2012; 17(6):801-12.
12. Pfeifer S, Fritz M, Goldberg J. et al. Practice Committee Opinion of the American Society of Reproductive Medicine: Evaluation and treatment of recurrent pregnancy loss: a committee opinion. Fertil Steril. 2012; 98: 1103-11.
13. Prior TW, Russman BS. Spinal muscular atrophy. Includes: arthrogryposis multiplex congenita-spinal muscular atrophy (AMC-SMA), congenital axonal neuropathy (CAN), spinal muscular atrophy 0 (SMA0), spinal muscular atrophy I (Werdnig-Hoffmann disease, SMA I), spinal muscular atrophy II (SMA II), spinal muscular atrophy III (Kugelberg-Welander disease, SMA III), spinal muscular atrophy IV (SMA IV) [Internet] GeneReviews. 2013 Nov Accessed at: http://www.ncbi.nlm.nih.gov/books/NBK1352/ Accessed 7/29/2016.
14. Schmidt KT, Andersen CY, ISFP Practice Committee. Recommendations for fertility preservation in patients with lymphomas. Journal of Assisted Reproduction and Genetics 2012;29(6):473-7.
15. Traeger-Synodinos J, Vrettou C, Kanavakis E. Prenatal, noninvasive, and preimplantation genetic diagnosis of inherited disorders: hemoglobinopathies.Traeger-Synodinos J - Expert

Rev Mol Diagn. Apr 2011; 11(3): 299-312.
16. Van Rij MC. Preimplantation genetic diagnosis (PGD) for Huntington's disease: the experience of three European centres - Eur J Hum Genet/ Apr 2012; 20(4): 368-75.
17. BJJorn; Ingerslev, Hans Jakob; Lemmen, Josephine Gabriela; Degn, Birte; Rasmussen, Iben Anne; Kesmodel, Ulrik Schioler. Original article: Preimplantation genetic diagnosis: a national multicenter obstetric and neonatal follow-up study. Fertility and Sterility. November 2016 106(6): 1363-1369 e1 DOI: 0.1016/j. fertnstert.2016.07.109.
18. The use of preimplantation genetic testing for aneuploidy (PGT-A): a committee opinion. American Society of Reproductive Medicine and Society for Assisted Reproductive Technology. FertilSteril 2018; 109:429-36.21.
19. Chen, Hsin-Fu; Chen, Shee-Uan; Ma, Gwo-Chin; Hsieh, Sung-Tsang; Tsai, Horng-Der; Yang, Yu-Shih; Chen, Ming. Preimplantation genetic diagnosis and screening: Current status and future challenges. Journal of the Formosan Medical Association. February 2018 117(2):94-100 Language: English. DOI: 10.1016/j.jfma.2017.08.006, Database: ScienceDirect.
20. Asscher E., Koops, BJ. The right not to know and preimplantation genetic diagnosis for Huntington's disease. J Med Ethics. 2010 Jan;36(1):30-3. doi: 10.1136/jme.2009.031047.
21. Capalbo A, Romanelli V, Cimadomo D, Girardi L, Stoppa M, Dovere L, Dell'Edera D, Ubaldi FM, Rienzi L. Implementing PGD/PGD-A in IVF clinics: considerations for the best laboratory approach and management. J Assist Reprod Genet. 2016 Oct;33(10):1279-1286. Epub 2016 Jul 16. DOI: 10.1007/s10815-016-0768-3.
22. Benard, J., Targa, C., Murisier, F., Paoloni-Giacobino, A., & Streuli, I. (2019). Gynécologie-obstétrique: Tests préimplantatoires de l'embryonen médecine de reproduction [Preimplantation genetic testing]. Revue medicale suisse, 15(N° 632-633), 53–56. https://pubmed.ncbi.nlm.nih.gov/30629370/
23. Chan, Y. M., Li, T. C., & Poon, L. (2019). Impact of preimplantation genetic testing for aneuploidy on obstetrical practice. Current opinion in obstetrics & gynecology, 31(2), 127–131. https://doi.org/10.1097/GCO.0000000000000521
24. Palmerola, K. L., Vitez, S. F., Amrane, S., Fischer, C. P., & Forman, E. J. (2019). Minimizing mosaicism: assessing the impact of fertilization method on rate of mosaicism after next-generation sequencing (NGS) preimplantation genetic testing for aneuploidy (PGT-A). Journal of assisted reproduction and genetics, 36(1), 153–157. https://doi.org/10.1007/s10815-018-1347-6
25. Patrizio, P., Shoham, G., Shoham, Z., Leong, M., Barad, D. H., & Gleicher, N. (2019). Worldwide live births following the transfer of chromosomally "Abnormal" embryos after PGT/A: results of a worldwide web-based survey. Journal of assisted reproduction and genetics, 36(8), 1599–1607. https://doi.org/10.1007/s10815-019-01510-0
26. Medscape Drugs & Diseases > Obstetrics & Gynecology. Preimplantation Genetic Diagnosis Updated: Aug 29, 2018, Author: Molina B Dayal, MD, MPH; Chief Editor: Richard Scott Lucidi, MD, FACOG accessed 9.30/.2021
27. Practice Committee and Genetic Counseling Professional Group (GCPG) of the American Society for Reproductive Medicine. Clinical management of mosaic results from

preimplantation genetic testing for aneuploidy (PGT-A) of blastocysts: a committee opinion. *Fertility and Sterility*® Vol. 114, No. 2, August 2020 005-0282/$36.00 Copyright ©2020 American Society for Reproductive Medicine, https://doi.org/10.1016/j.fertnstert.2020.05.014

28. 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. *Fertility and Sterility*® Vol. 109, No. 3, March 2018 American Society for Reproductive Medicine, https://doi.org/10.1016/j.fertnstert.2018.01.002
29. Yan, J et al. Live Birth with or without Preimplantation Genetic Testing for Aneuploidy. *The New England Journal of Medicine*. November 2021. 385:2047-2058 DOI: 10.1056/NEJMoa2103613. https://www.nejm.org/doi/10.1056/NEJMoa2103613
30. Klugman, S., Rollene, N. Preimplantation Genetic Testing. American College of Obstetricians and Gynecologists (ACOG). Committee on Genetics. Number 799. March 2020. https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2020/03/preimplantation-genetic-testing
31. MCG 27th edition, Copyright © 2023 MCG Health, LLC, ACG: A-0812 (AC) Chromosomal Microarray Analysis (CMA) – Prenatal Testing Accessed 06/21/2023
32. Preimplantation Genetic Testing: ACOG Committee Opinion, Number 799. (2020). *Obstetrics and gynecology*, *135*(3), e133–e137. https://doi.org/10.1097/AOG.0000000000003714
33. Simopoulou, M., Sfakianoudis, K., Maziotis, E., Tsioulou, P., Grigoriadis, S., Rapani, A., Giannelou, P., Asimakopoulou, M., Kokkali, G., Pantou, A., Nikolettos, K., Vlahos, N., & Pantos, K. (2021). PGT-A: who and when? A systematic review and network meta-analysis of RCTs. *Journal of assisted reproduction and genetics*, *38*(8), 1939–1957. https://doi.org/10.1007/s10815-021-02227-9
34. Tiegs, A. W., Tao, X., Zhan, Y., Whitehead, C., Kim, J., Hanson, B., Osman, E., Kim, T. J., Patounakis, G., Gutmann, J., Castelbaum, A., Seli, E., Jalas, C., & Scott, R. T., Jr (2021). A multicenter, prospective, blinded, nonselection study evaluating the predictive value of an aneuploid diagnosis using a targeted next-generation sequencing-based preimplantation genetic testing for aneuploidy assay and impact of biopsy. *Fertility and sterility*, *115*(3), 627–637. https://doi.org/10.1016/j.fertnstert.2020.07.052

Approval History

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Date approved by RUMC*	Date filed with the State of Maryland	Effective Date (Ten days after filing)
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08/27/2015	08/282015	09/08/2015

Approval History

Effective June 01, 2016, state filing no longer required per Maryland House Bill HB 798 – Health Insurance – Reporting

Date approved by RUMC	Date of Implementation
09/13/2016	09/13/2016
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*The Regional Utilization Management Committee received *delegated authority* from the Regional Quality Improvement Committee to review and approve designated Utilization Management and Medical Coverage Policies in 2011.

Note: Kaiser Permanente Mid-Atlantic States (KPMAS) include referral and authorization criteria to support primary care and specialty care practitioners, as appropriate, in caring for members with selected conditions. Whenever possible, Medical Coverage Policies are evidence-based and may also include expert opinion. Medical Coverage Policies are not intended or designed as a substitute for the reasonable exercise of independent clinical judgment by a practitioner in any particular set of circumstances for an individual member.