KAISER PERMANENTE®

**Kaiser Foundation Health Plan of Washington**

# *Clinical Review Criteria*
# Cell-Free Fetal DNA Analysis

- Panorama
- MaterniT21™
- Harmony™
- Verifi™
- QNatal Advanced



## Criteria

***Preferred Lab for Genetic Testing for Kaiser Permanente non-Medicare enrollees (for in-network coverage)***

*Prevention and Invitae Corporation is the preferred lab for genetic testing* when the test(s) is/are available at Prevention or Invitae and medical necessity criteria are met.*

*Invitae's test catalog can be found here: Invitae Test Catalog*
*Prevention test catalog can be found here: Prevention Test Catalog*

**Note: This does not affect processing of tumor or other pathology specimens as they are not performed by Invitae.*

*PPO/POS members may use non-preferred labs at the out of network cost share.*

***Exceptions***

*For the genetic test(s) listed below, please use the lab specified:*

- ***Cell Free Fetal DNA testing* –Any of these three labs can be used:**
  - *Ariosa Diagnostics, Inc. (81507)*
  - *Invitae (81420)*
  - *LabCorp (81420)*
  - *Quest-QNatal (81420)*

### For Medicare Members

| Source | Policy |
|---|---|
| CMS Coverage Manuals | None |
| National Coverage Determinations (NCD) | None |
| Local Coverage Determinations (LCD) | Molecular Diagnostic Tests (L36256) |
| Local Coverage Article | None |

### For Non-Medicare Members



Back to Top

Kaiser Permanente will cover cell-free fetal DNA testing for trisomies without clinical review for pregnant women regardless of age when performed at Ariosa Diagnostics (CPT code 81507) or at Invitae (CPT code 81420) or at Labcorp (CPT code 81420) or at Quest-QNatal (81420).

Prior Authorization will still be required for Non-Invasive Prenatal Testing (NIPT) at any other lab in advance of submitting a claim for payment. For patients who are tested for trisomies using cell-free fetal DNA, the sequential screen and nuchal translucency (NT) ultrasound (76813/76814) should no longer be routinely ordered without clinical indication.

The only codes that Kaiser Permanente will pay for Cell-Free Fetal DNA Analysis for Trisomies are 81420 and 81507.

**Considered not medically necessary:**

| Test Name | Criteria Used | Codes |
|---|---|---|
| Cell-Free Fetal DNA - Microdeletion Syndromes | A-0848: This service is not covered per MCG guidelines | CPT – 81331 *not medically necessary when performed using cell-free fetal DNA*, 81422 |
| Cell-Free Fetal DNA - Monogenic Disorders | A-0849: This service is not covered per MCG guidelines | CPT – 81479 |
| Cell-Free Fetal DNA - Sex Chromosome Disorders | A-0850: This service is not covered per MCG guidelines. | CPT – 81479 |

**If requesting review for these services, please send the following documentation:**

- Last 6 months of clinical notes from requesting provider &/or specialist

***MCG Manuals are proprietary and cannot be published and/or distributed.** However, on an individual member basis, Kaiser Permanente can share a copy of the specific criteria document used to make a utilization management decision. If one of your patients is being reviewed using these criteria, you may request a copy of the criteria by calling the Kaiser Permanente Clinical Review staff at 1-800-289-1363.

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

## Background

Fetal chromosomal abnormalities occur in approximately 1 in 160 live births. Most fetal chromosomal abnormalities are aneuploidies, defined as an abnormal number of chromosomes. The trisomy syndromes are aneuploidies involving 3 copies of 1 chromosome. The most important risk factor for trisomy syndromes is maternal age. The approximate risk of a trisomy 21 (T21; Down syndrome) –affected birth is 1 in 1100 at age 25 to 29. The risk of a fetus with T21 (at 16 weeks of gestation) is about 1 in 250 at age 35 and 1 in 75 at age 40.1

T21 is the most common chromosomal aneuploidy and provides the impetus for current maternal serum screening programs. Other trisomy syndromes include T18 (Edwards syndrome) and T13 (Patau syndrome), which are the next most common forms of fetal aneuploidy, although the percentage of cases surviving to birth is low and survival beyond birth is limited. The prevalence of these other aneuploidies is much lower than the prevalence of T21 and identifying them is not currently the main intent of prenatal screening programs. Also, the clinical implications of identifying T18 and 1T3 are unclear because survival beyond birth is limited for both conditions.

Standard aneuploidy screening involves combinations of maternal serum markers and fetal ultrasound done at various stages of pregnancy. The detection rate for various combinations of noninvasive testing ranges from 60% to 96% when the false-positive rate is set at 5%. When tests indicate a high risk of a trisomy syndrome, direct karyotyping of fetal tissue obtained by amniocentesis or chorionic villous sampling (CVS) is required to confirm that T21 or another trisomy is present. Both amniocentesis and CVS are invasive procedures and have an associated risk of miscarriage. A new screening strategy that reduces unnecessary amniocentesis and CVS procedures and increases detection of T21, T18, and T13 could improve outcomes. Confirmation of positive


Back to Top

noninvasive screening tests with amniocentesis or CVS is recommended; with more accurate tests, fewer women would receive positive screening results.

Commercial, noninvasive, sequencing-based testing of maternal serum for fetal trisomy syndromes is now available. The test technology involves detection of cell-free fetal DNA fragments present in the plasma of pregnant women. As early as 8 to 10 weeks of gestation, these fetal DNA fragments comprise 6% to 10% or more of the total cell-free fetal DNA in a maternal plasma sample. The tests are unable to provide a result if the fetal fraction is too low (ie, <4%). Fetal fraction can be affected by maternal and fetal characteristics. For example, fetal fraction was found to be lower at higher maternal weights and higher with increasing fetal crown-rump length.

## Medical Technology Assessment Committee (MTAC)

***MaterniT21***

**08/20/2012: MTAC REVIEW**

**Evidence Conclusion:** Kaiser identified two observational studies that evaluated MaterniT21. The first study was a case-control study that evaluated 212 samples with by trisomy 21 matched with 1,483 euploid samples, 62 samples with trisomy 18 matched with 183 euploid samples, and 12 samples with trisomy 13 matched with 36 euploid samples. All of the samples were taken from women at high-risk for fetal aneuploidy. Before adjustment the test had a sensitivity of 98.6% and a false positive rate of 0.2% for detecting trisomy 21. After adjusting for guanine cytosine content and removing repetitive regions, the test had a sensitivity of 99.1% and a false positive rate of 0.1% for diagnosing trisomy 21. After adjustment for guanine cytosine content the test had a sensitivity of 100% and a false positive rate of 0.3% for diagnosing trisomy 18, and a sensitivity of 91.7% and a false positive rate of 0.9% for diagnosing trisomy 13 (Palomaki 2011, Palomaki 2012). The second study was a cohort study that included 480 samples from women at high-risk for fetal aneuploidy. Results from this study suggest that before adjusting for guanine cytosine content and removing repetitive regions this test has a sensitivity of 100% and a false positive rate of 0.2% (Ehrich 2011). Based on this evidence Kaiser concluded that despite a promising diagnostic performance, MaterniT21 suffers from an extremely sparse, vendor-involved body of evidence specific to a high-risk population, and lacks studies examining the prospective impact of MaterniT21 on patients' decisions of whether to purse chorionic villus sampling or amniocentesis (Kaiser 2012). *Conclusion*: Kaiser concluded that there is insufficient evidence to determine whether the MaterniT21 prenatal test to detect Down syndrome is medically appropriate for any patient.

**Articles**: In March 2012, Kaiser review MaterniT21 for the detection of trisomy 21. No additional studies were identified since the Kaiser review. The following technology assessment was selected for review: Kaiser Permanente. Sequenom's MaterniT21 prenatal test to detect Down syndrome. March 2012. http://cl.kp.org/pkc/national/cpg/intc/materials/MaterniT21toDetectTrisomy21(G121107).pdf.

The use of MaterniT21 does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

## Applicable Codes

**Considered Medically Necessary when criteria in the applicable policy statements listed above are met:**

| CPT® Codes | Description |
|---|---|
| **81420** | Fetal chromosomal aneuploidy (eg, trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal blood, must include analysis of chromosomes 13, 18, and 21 |
| **81507** | Fetal aneuploidy (trisomy 21, 18, and 13) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy |

**Considered Not Medically Necessary when performed using cell-free fetal DNA:**

| CPT® Codes | Description |
|---|---|
| **81331** | SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (eg, Prader-Willi syndrome and/or Angelman syndrome), methylation analysis |
| **81403** | Molecular Pathology Procedure Level 4 |
| **81422** | Fetal chromosomal microdeletion(s) genomic sequence analysis (eg, DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood |
| **81479** | Unlisted molecular pathology procedure |


Back to Top

***Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

******To verify authorization requirements for a specific code by plan type, please use the **Pre-authorization Code Check**.



| Date Created | Date Reviewed | Date Last Revised |
|---|---|---|
| 09/04/2012 | 09/04/2012[MDCRPC], 10/02/2012[MDCRPC], 02/05/2013[MDCRPC], 1, 03/01/2022[MPC] 2/03/2013[MPC], 01/07/2014[MPC], 11/04/2014[MPC], 09/01/2015[MPC], 07/05/2016[MPC], 05/02/2017[MPC], 03/06/2018[MPC], 03/05/2019[MPC], 03/03/2020[MPC], 03/02/2021[MPC], 03/01/2022[MPC],03/07/2023[MPC] | 04/24/2023 |

[MDCRPC] Medical Director Clinical Review and Policy Committee
[MPC] Medical Policy Committee

| Revision History | Description |
|---|---|
| 09/08/2015 | Revised LCD L34101 |
| 07/05/2016 | Adopted GHC-0724 |
| 04/08/2020 | Added temporary change for code 81507 due to COVID-19 pandemic |
| 06/02/2020 | Extended temporary change until September 15, 2020 for code 81507 due to COVID-19 pandemic |
| 08/04/2020 | Extended temporary change until November 1, 2020 for code 81507 due to COVID-19 pandemic |
| 12/07/2020 | Extended temporary change until February 15, 2021 for code 81507 due to COVID-19 pandemic |
| 03/08/2021 | Extended temporary change until May 15, 2021 for code 81507 due to COVID-19 pandemic |
| 05/04/2021 | Extended temporary change until June 15, 2021 for code 81507 due to COVID-19 pandemic |
| 06/01/2021 | Extended temporary change until August 15, 2021 for code 81507 due to COVID-19 pandemic |
| 08/03/2021 | MPC approved to permanently eliminate age restrictions on cell-free fetal DNA (NIPT) testing for trisomies for commercial members (81507 and 81420). Prior authorization is still required for this testing at labs other than Ariosa. Requires 60-day notice, effective date January 1, 2022. Extended temporary change until December 31, 2021 for code 81507 due to COVID-19 pandemic. |
| 03/01/2022 | Updated applicable codes. |
| 08/16/2022 | MCG* A-0847 was removed from the 26th edition; removed from criteria |
| 10/7/2022 | Added labcorp as preferred vendor for Cell Free Fetal DNA testing. Noted Prevention as preferred lab for genetic testing. |
| 04/24/2023 | Added Quest-QNatal as a preferred vendor for Cell Free Fetal DNA testing. |



Back to Top