



INDIANA HEALTH COVERAGE PROGRAMS

PROVIDER REFERENCE MODULE

Genetic Testing

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1.0	Policies and procedures as of October 1, 2015 Published: February 25, 2016	New document	FSSA and HPE
1.1	Policies and procedures as of April 1, 2016 Published: October 18, 2016	Semiannual update: <ul style="list-style-type: none"> • Edited text throughout for clarity • Added a note box for managed care contact information • Changed references to the prior authorization contractor from ADVANTAGE Health Solutions to Cooperative Managed Care Services (CMCS) • Updated information in the Chromosomal Microarray Analysis Genetic Testing section • Updated information in the BRCA 1 and BRCA 2 Genetic Testing for Breast and Ovarian Cancer section • Updated test names and billing code in the Genetic Testing for the Management of Breast Cancer section • Added the JAK2 Gene Analysis section 	FSSA and HPE

Table of Contents

Introduction.....	1
Prior Authorization for Genetic Testing.....	1
Coverage and Billing for Genetic Testing.....	2
Chromosomal Microarray Analysis Genetic Testing.....	2
Cytogenetics.....	4
Genetic Testing for Cancer Susceptibility	4
Genetic Testing for the Management of Breast Cancer	6
Genetic Testing Panels.....	7
JAK2 Gene Analysis.....	7
Molecular Pathology.....	7
Multianalyte Assays with Algorithmic Analyses.....	8

Note: For policy information regarding coverage of genetic testing, see the [Medical Policy Manual](#) at [indianamedicaid.com](#).

Introduction

The Indiana Health Coverage Programs (IHCP) implemented a new general policy regarding coverage of genetic testing services, effective January 1, 2015. This policy addresses IHCP coverage of genetic testing services overall. Coverage policies issued regarding specific genetic tests or techniques supplement this policy.

Prior authorization (PA), coverage, reimbursement, and billing information in this document applies to services provided under the fee-for-service (FFS) delivery system. Within the managed care delivery system, individual managed care entities (MCEs) establish and publish PA, reimbursement, and billing criteria.

Note: For Healthy Indiana Plan (HIP), Hoosier Care Connect, and Hoosier Healthwise members, providers must contact the appropriate managed care entity (MCE) for specific policies and procedures. MCE contact information is included in the [IHCP Quick Reference Guide](#) available at [indianamedicaid.com](#).

Prior Authorization for Genetic Testing

PA for genetic testing is always required, unless otherwise noted within the [Fee Schedule](#) at [indianamedicaid.com](#) or by a test-specific coverage policy.

PAs are test-specific, and providers must follow all available guidelines established by the American College of Medical Genetics. If no guidelines are available, providers should follow commonly accepted medical guidelines, such as Amsterdam II or revised Bethesda guidelines for hereditary nonpolyposis colorectal cancer (HNPCC) diagnoses. All IHCP policy guidelines must also be met for PA approval. The following documentation is required for PA review:

- Documentation outlining medical necessity, specifically stating the impact on the patient's treatment
- Documentation that genetic counseling has been performed prior to testing
- Results from any commonly used conventional diagnostic testing showing inconclusive diagnosis
- All other general documentation required for PA

Questions about FFS PA should be directed to Cooperative Managed Care Services (CMCS) at 1-800-269-5720. Questions about PA for managed care members should be directed to the MCE with which the member is enrolled.

Coverage and Billing for Genetic Testing

The IHCP provides coverage for a variety of genetic tests when provided in compliance with IHCP coverage and billing guidelines. All the following circumstances must apply for any genetic testing service to be covered:

- The genetic disorder must be associated with a potentially significant disability.
- The risk of the significant disability from the genetic disorder cannot be identified through biochemical or other testing (for example, ultrasound screening for aortic disease in Marfan's syndrome).
- A specific mutation, or set of mutations, has been established in scientific literature to be reliably associated with the disease.
- The results of the genetic test could impact the medical management of the member with improved net-health outcomes.
- No determinable diagnosis can be gathered from the history, physical examination, pedigree analysis, genetic counseling, and completion of conventional diagnostic studies.
- Prior authorization is obtained, if required.

Genetic testing services are *not* covered under the following circumstances:

- Testing for the sole convenience of information for the patient without impacting treatment
- All screening tests, except the screening tests listed under the State's required newborn screening policy (see *Indiana Administrative Code 410 IAC 3-3-3* or the [Inpatient Hospital Services](#) module for the list of required newborn screening tests)
- Tests performed for the medical management of other family members, unless otherwise specified in policy
- History, physical examination, pedigree analysis, genetic counseling, or completion of conventional diagnostic studies has given a definitive diagnosis
- A genetic test was previously performed for the member to provide a conclusive diagnosis of the same genetic disorder
- Testing to establish paternity

Genetic tests specific to a gene or a condition are limited to once per member, per lifetime, unless otherwise specified in a test-specific coverage policy. For genetic tests not specific to a gene or a condition, providers must have medical documentation on file, indicating that each testing procedure is for a separate and distinct diagnosis.

The following subsections include additional coverage guidelines for certain categories of genetic testing.

Chromosomal Microarray Analysis Genetic Testing

The IHCP covers chromosomal microarray analysis (CMA) genetic testing. Coverage applies to all IHCP programs, subject to limitations established for certain benefit packages and in accordance with the policies and procedures described in this document.

Coverage Parameters

CMA testing is considered a first-line test in postnatal evaluation of members with unexplained developmental delay/intellectual delay (DD/ID) or autism spectrum disorder (ASD) and multiple cognitive abnormalities not specific to a well-defined genetic syndrome. The IHCP covers CMA testing when it is

determined to be medically necessary for diagnosing a genetic abnormality in children with apparent nonsyndromic cognitive DD/ID or ASD, according to the latest accepted *Diagnostic and Statistical Manual of Mental Disorders* guidelines.

CMA testing is **not** considered medically necessary and will **not** be covered under the following circumstances:

- To confirm the diagnosis of a disorder or syndrome that is routinely diagnosed based on clinical evaluation alone
- For prenatal genetic testing
- For the screening, diagnosis, and management of hematologic or oncologic malignancies
- As a means to predict or evaluate pregnancy loss
- In cases of family history of chromosome rearrangement in a phenotypically normal individual
- In all other cases of suspected genetic abnormality in children with DD/ID or ASD

Billing Guidelines

The IHCP reimburses for CMA testing when billed with the appropriate Current Procedural Terminology (CPT^{®1}) code:

- 81228 – *Cytogenetic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (e.g., Bacterial Artificial Chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)*
- 81229 – *Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities*

CMA testing is limited to one unit per recipient, per lifetime. Testing cannot be reported using a combination of molecular diagnostic codes (83890–83913) and array-based evaluation of molecular probes codes (88384–88386).

Prior Authorization Requirements

The IHCP requires PA for CMA testing. To obtain PA for CPT codes 81228 or 81229, **all** the following conditions must be met:

- Any indicated biochemical tests for metabolic disease have been performed, and results are nondiagnostic.
- FMR1 gene analysis (for Fragile X), when clinically indicated, is negative.
- In addition to a diagnosis of nonsyndromic DD/ID or ASD, the child has **one or more** of the following (see definitions following the requirements):
 - Two or more major malformations
 - A single major malformation or multiple minor malformations in an infant or child who is also small-for-dates
 - A single major malformation and multiple minor malformations
- The results for the genetic testing have the potential to impact the clinical management of the patient.
- Testing is requested after the parents have been engaged in face-to-face genetic counseling with a healthcare professional who is licensed under *Indiana Code IC 25-17.3*.

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Note: The following definitions from the American College of Medical Genetics Guidelines, Evaluation of the Newborn with Single or Multiple Congenital Abnormalities apply to the IHCP PA policy for CMA testing:

- A **malformation** refers to abnormal structural development.
- A **major malformation** is a structural defect that has a significant effect on function or social acceptability, such as ventricular septal defect or cleft lip.
- A **minor malformation** is a structural abnormality that has a minimal effect on function or social acceptance, such as preauricular ear pit or partial syndactyly (fusion) of the second or third toes.
- A **syndrome** is a recognizable pattern of multiple malformations. Syndrome diagnoses are often relatively straightforward and common enough to be clinically recognized without specialized testing. Examples include Down syndrome, neural tube defects, and achondroplasia. However, in the very young or in the case of symptoms with variable presentation, confident identification may be difficult without additional testing.

Cytogenetics

The National Human Genome Research Institute defines *cytogenetics* as “the branch of genetics that studies the structure of DNA within the cell nucleus.” Cytogenetics studies the number and morphology of chromosomes, using chromosome banding techniques (classical cytogenetics) or hybridization fluorescently labeled probes (molecular cytogenetics).

Most cytogenetic tests are IHCP-covered services. To be covered, these tests must meet the general criteria previously stated as well as all test-specific guidelines established by the American College of Medical Genetics.

Genetic Testing for Cancer Susceptibility

Several genetic tests exist for a determination or risk score associated with inheritable cancer susceptibility, such as breast and ovarian cancer (BRCA) or hereditary nonpolyposis colorectal cancer (HNPCC). Providers should check the [Fee Schedule](#) at indianamedicaid.com for coverage of specific tests. Cancer-susceptibility genetic testing is a covered service when the general criteria **and both** the following conditions are met:

- A specific mutation, or set of mutations, has been established in the scientific literature to be reliably associated with the risk of developing malignancy.
- The results of the genetic test potentially affect at least one of the management options considered by the referring, ordering, or treating physician, in accordance with accepted standards of medical care, including any one of the following:
 - Surgery, or the extent of surgery
 - A change in surveillance
 - Hormonal manipulation
 - A change in standard therapeutic or adjuvant chemotherapy

All criteria set forth in test-specific coverage policies must also be met.

HER2 Laboratory Breast Cancer Testing

The *Procedure Codes for HER2 Tests* table in the *Genetic Testing Codes* on the [Code Sets](#) page at indianamedicaid.com lists the CPT codes providers should use to bill the HER2 protein over expression test, HercepTest®, as an aid in assessing patients who use trastuzumab, HERCEPTIN®.

HER2/neu gene detection tests, such as Oncor's INFORM®, is an adjunct to existing clinical and pathological information and an aid to stratify breast cancer patients with a primary, invasive, or localized breast cancer, who are lymph node negative, for risk of recurrence or disease-related death. Providers use these tests as a prognostic indicator and should use the CPT codes listed on the *Procedure Codes for HER2/neu Gene Detection Tests* table in the *Genetic Testing Codes* on the [Code Sets](#) page at indianamedicaid.com.

BRCA 1 and BRCA 2 Genetic Testing for Breast and Ovarian Cancer

The IHCP reimburses for genetic testing for breast and ovarian cancer (BRCA) 1 and BRCA 2 genetic testing when medically necessary, with PA, billed with the appropriate HCPCS and CPT codes listed on the *Procedure Codes to Report Genetic Testing for Breast and Ovarian Cancer Diagnoses Only* table in the *Genetic Testing Codes* on the [Code Sets](#) page at indianamedicaid.com. The IHCP reimburses the manually priced genetic test codes at 90% of billed charges.

Consistent with coding guidelines, providers may be reimbursed once per lifetime, per member, for only one of the CPT procedure codes in the following code pairs:

- 81211 or 81214
- 81211 or 81216
- 81211 or 81162
- 81162 or 81214
- 81162 or 81216

If both codes in the code pair are billed, one of the codes will be denied with an explanation of benefits (EOB) 6367 – *A BRCA analysis procedure is already paid for this date of service and only one procedure is allowed per lifetime*. Additionally, if the IHCP has provided reimbursement for CPT code 81162, 81211, 81214, or 81216, the IHCP will not reimburse 81212, 81213, 81215, or 81217 for that member because 81162, 81211, 81214, and 81216 represent *complete* BRCA 1 and/or BRCA 2 gene sequence analysis.

The IHCP gives PA for genetic testing related to breast and ovarian cancer (procedure codes listed on the *Procedure Codes to Report Genetic Testing for Breast and Ovarian Cancer Diagnoses Only* table) when medically necessary in the following circumstances. Providers must submit documentation with the PA request and must maintain it in the member's medical record.

- Clinically affected members (invasive breast cancer or ovarian cancer at any age) meeting at least one of the following criteria:
 - One or more first-degree (mother, father, sister, or daughter) or second-degree (aunt, uncle, grandmother, niece, or granddaughter) relatives with invasive breast cancer diagnosed before age 50
 - One or more first- or second-degree relatives with ovarian cancer
 - One or more first- or second-degree relatives with male breast cancer
- Members with a personal history of at least one of the following (no family history required):
 - Invasive breast cancer before age 50
 - Ovarian cancer at any age
 - Both invasive breast cancer *and* ovarian cancer at any age
 - Male breast cancer at any age

- Members with a family member (related by blood) with a known BRCA 1 or BRCA 2 mutation
- Members with Ashkenazi (Eastern European) Jewish ancestry with invasive breast cancer at any age, or meeting any of the previous criteria

The IHCP considers BRCA testing of men with breast cancer medically necessary for either of the following indications:

- To assess the man's risk of recurrent breast cancer
- To assess the breast cancer risk of a female member where the affected male is a first- or second-degree blood relative of that member

The IHCP considers BRCA 1 and BRCA 2 testing to assess the risk of breast or prostate cancer in men without breast cancer to be not medically necessary.

Genetic Testing for the Management of Breast Cancer

The IHCP covers Oncotype DX® Breast Recurrence Score genetic testing of breast cancer tumors when it is considered medically necessary for managing the treatment of breast cancer. The 21-gene RT-PCR assay should only be ordered after surgery and subsequent pathological examination of the tumor have been completed. The test should be ordered in the context of a provider-patient discussion regarding risk preferences when the test result will aid in making decisions regarding chemotherapy.

Noncovered Services

Gene expression profiling as a technique of managing the treatment of breast cancer is considered **investigational and not medically necessary** when a gene profiling test *other than* the Oncotype DX Breast Recurrence Score is being used, including but not limited to:

- Breast Cancer Gene Expression Ratio (also known as Theros H/ISM)
- Breast Cancer IndexSM
- Insight® DX Breast Cancer Profile
- MammaPrint® (also referred to as the “Amsterdam signature” or “70-gene signature”)
- Mammostrat®
- Oncotype DX Breast DCIS
- PAM50 Breast Cancer Intrinsic Classifier™
- The 41-gene signature assay
- The 76-gene “Rotterdam signature” assay

Gene expression profiling as a technique of managing the treatment of ductal carcinoma in situ (DCIS) is considered **investigational and not medically necessary** under all circumstances.

Repeat gene expression profiling with the Oncotype DX Breast Recurrence Score for the same tumor, such as a metastatic focus, or from more than one site when the primary tumor is multifocal is considered **investigational and not medically necessary**.

Oncotype DX Prior Authorization Requirements

The IHCP requires PA for Oncotype DX Breast Recurrence Score. To obtain PA for code 81519, **all** the following criteria must be met:

- Member has had surgery, and full pathological evaluation of the specimen has been completed.
- Histology is ductal, lobular, mixed, or metaplastic.
- Histology is not tubular or colloid.
- Estrogen receptor is positive (ER+), or progesterone receptor is positive (PR+), or both.
- HER2 receptor is negative.
- pN0 (node negative) or pN1mi with axillary lymph node micrometastasis is less than or equal to 2mm.
- Member has one of the following:
 - Tumor size 0.6–1.0 cm moderate/poorly differentiated
 - Tumor size 0.6–1.0 cm well-differentiated with any of the following unfavorable features: angiolymphatic invasion, high nuclear grade, or high histologic grade
 - Tumor size greater than 1.0 cm and less than or equal to 4.0 cm
- Member does not have a pT4 lesion.
- Chemotherapy is a therapeutic option being considered and will be supervised by the practitioner ordering the gene expression profile.

Gene expression profiling with the Oncotype DX Breast Recurrence Score as a technique of managing the treatment of breast cancer is considered **not medically necessary** when the criteria listed have not been met.

Genetic Testing Panels

Genetic testing panels are not covered.

JAK2 Gene Analysis

Effective April 1, 2015, the IHCP covers CPT code 81270 – *JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, p. Val617Phe (V617F) variant*. PA is required.

Molecular Pathology

Molecular pathology procedures are medical laboratory procedures involving analyses of nucleic acid to achieve the following:

- Detect variants in genes that may be indicative of one of the following:
 - Germ line (for example, constitutional disorders)
 - Somatic conditions (for example, neoplasia)
- Test for histocompatibility antigens, such as the human leukocyte antigen (HLA)

Many molecular genetic tests are IHCP-covered services. To be covered, these tests must meet the general criteria previously stated as well as all test-specific guidelines established by the American College of Medical Genetics.

Multianalyte Assays with Algorithmic Analyses

Multianalyte Assays with Algorithmic Analyses (MAAAs) are procedures that use multiple results derived from assays of various types, including molecular pathology assays, fluorescent in situ hybridization assays, and non-nucleic acid-based assays, such as proteins, polypeptides, lipids, and carbohydrates. Algorithmic analysis using the results of these assays as well as other patient information is then performed and reported typically as a numeric score or a probability.

In general, MAAA procedures are noncovered services, because they do not provide a definitive diagnosis or change the course of treatment. Policy exceptions may be established for specific MAAA procedures.