Subject: Whole Genome Sequencing

Background: Harvard Pilgrim Health Care has delegated utilization management of whole genome sequencing testing to AIM Specialty Health (AIM)

Whole genome sequencing (WGS) is the analysis of the DNA content individual’s genome, used to establish a diagnosis in individuals with especially complex and severe phenotypes. In the pediatric outpatient setting, when either whole exome sequencing (WES) or CMA is being considered, patients may benefit from the broader testing capability provided by WGS. Given these benefits, HPHC covers WGS for individuals under 18 years of age in the outpatient setting who meet AIM whole exome sequencing (WES) guideline criteria. WGS is recommended over either WES or CMA in this population.

Authorization: Prior authorization is required for whole genome sequencing provided to members enrolled in commercial (HMO, POS, PPO), products through AIM Specialty Health

Policy and Coverage Criteria:

Whole Genome Sequencing
Whole Genome Sequencing in members under the age of 18 in the outpatient setting, (81425 when performed with or without 81426), is considered medically necessary when ALL of the following criteria are met:

- The member meets coverage criteria for whole exome sequencing outlined in the AIM GUTM Guideline: Whole Exome and Whole Genome Sequencing (see exclusions below) and below General Eligibility criteria are met
- The member/ guardian has completed genetic counseling and has been referred for genetic testing by one of the following:
  - An independent board-certified or board eligible medical geneticist not employed by a commercial genetic testing laboratory*
  - An American Board of Medical Geneticist or American Board of Genetic Counseling-certified genetic counselor not employed by a commercial genetic testing laboratory*
  - A genetic nurse credentialed as either the Genetic Nursing Credentialing Commission (GNCC) or the American Nurses Credentialing Center (ANCC) who is not employed by a commercial genetic testing laboratory*
  - Who:
    - Has evaluated the case and performed pre-test genetic counseling
    - Has completed a three-generation pedigree
    - Intends to engage in post-test follow-up genetic counseling

* A physician, genetic counselor or genetic nurse employed by a laboratory that operates within an integrated, comprehensive healthcare delivery system is not considered to be an employee of a commercial genetic testing laboratory for the purpose of these guidelines

Fetal testing and testing in adults (older than 18 years of age) using WGS is excluded from coverage. Inpatient testing in the pediatric population (e.g. NICU/PICU) is not within the scope of this program.

General Eligibility Criteria:
- Results from WGS will directly impact clinical decision-making and/or clinical outcome
- No other causative circumstances (e.g., environmental exposures, injury, prematurity, infection) can explain symptoms
- Clinical presentation does not fit a well-described syndrome for which single-gene or targeted panel testing is available
- The differential diagnosis list and/or phenotype warrant testing of multiple genes, and at least one of the following:
  - WGS is more practical than the separate single gene tests or panels that would be recommended based on the differential diagnosis
  - WGS results may preclude the need for multiple and/or invasive procedures, follow-up, or screening (diagnostic odyssey) that would be recommended in the absence of testing

**Exclusions:** Harvard Pilgrim Health Care (HPHC) considers whole genome sequencing as not medically necessary for all other indications. In addition, HPHC does not cover:
- Testing using cell-free DNA
- Preimplantation testing of an embryo
- Genetic carrier screening
- Oncology indications
- Personal and family history of neurological features is excluded from coverage unless additional criteria are met
- Inpatient testing

**Coding:**
Codes are listed below for informational purposes only, and do not guarantee member coverage or provider reimbursement. The list may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible.

<table>
<thead>
<tr>
<th>CPT® Code</th>
<th>Description</th>
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<tr>
<td>81425</td>
<td>Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis</td>
</tr>
<tr>
<td>81426</td>
<td>Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator genome (eg, parents, siblings) (List separately in addition to code for primary procedure)</td>
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<tr>
<td>81427</td>
<td>Genome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained genome sequence (eg, updated knowledge or unrelated condition/syndrome)</td>
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**Billing Guidelines:**
Member's medical records must document that services are medically necessary for the care provided. Harvard Pilgrim Health Care maintains the right to audit the services provided to our members, regardless of the participation status of the provider. All documentation must be available to HPHC upon request. Failure to produce the requested information may result in denial or retraction of payment.

**Summary of Changes:**

<table>
<thead>
<tr>
<th>Date</th>
<th>Change</th>
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<tbody>
<tr>
<td>11/20</td>
<td>New Policy</td>
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Approved by Medical Policy Committee: 11/10/20
Approved by Clinical Policy Operational Committee: 11/20
Policy Effective Date: 01/01/2021
Initiated: 11/2020