# Genetic Testing for Angelman and Prader-Willi Syndromes

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**Line of Business:** Commercial

## Medical Coverage Policy

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## Related Medical/Pharmacy Coverage Policies

Genetic Testing

## Description

Angelman syndrome (AS) is a neurogenic genetic disorder characterized by developmental delay, intellectual disability, lack of speech, seizures and walking and balance disorders. Prader-Willi syndrome (PWS) is a genetic disorder characterized by hypogonadism, hypotonia (weak muscle tone), intellectual disability, short stature and an uncontrolled appetite that leads to life-threatening obesity.

The diagnosis of AS or PWS can be established through a variety of biochemical and genetic tests including deoxyribonucleic acid (DNA) methylation analysis, chromosomal microarray (CMA) (also referred to as comparative genomic hybridization [CGH]), sequence analysis, deletion/duplication analysis, fluorescent in situ hybridization (FISH), uniparental disomy (UPD) and imprinting defect (ID) studies.

## Coverage Determination

**Any state mandates for genetic testing take precedence over this medical coverage policy.**

**Genetic testing may be excluded by certificate. Please consult the member's individual certificate regarding Plan coverage.**

**Angelman Syndrome**

Humana members may be eligible under the Plan for **genetic testing to confirm a diagnosis of AS** when the following criteria are met:

- Pre- and post-test genetic counseling; **AND**
- Presence of developmental delay or intellectual disability as defined by the presence of impaired intellectual and adaptive functioning in at least 1 adaptive domain; **AND**
- Presence of gait ataxia and/or tremulous movement of the limbs; **AND**
- Presence of severe speech impairment; **AND**
- Presence of unique behavior with inappropriate happy demeanor that includes frequent laughing, smiling and excitability

**AS Testing Strategy:**

- Testing begins with DNA methylation analysis of the 15q11.2 – q13 chromosome region (eg, *UBE3A* gene)
    - If DNA methylation analysis is normal and suspicion for AS remains, then proceed to *UBE3A* sequence analysis, **OR**
    - If DNA methylation analysis is pathogenic or a likely pathogenic variant is identified, then proceed to CMA/CGH gene-targeted analysis
        - If CMA/CGH analysis is normal, then proceed to UPD study
        - If UPD is normal, then proceed to ID study

**Prader-Willi Syndrome**

Humana members may be eligible under the Plan for **genetic testing to confirm a diagnosis of PWS** when the following criteria are met:

- Pre- and post-test genetic counseling; **AND**
- Individual is between birth through 1 year of age with the following characteristics:

- Hypotonia with poor suck; **OR**

- Individual is between 2 through 5 years of age with the following characteristics:
  - Global developmental delays (GDD) as defined by the presence of delay in at least 2 developmental domains*****; **AND**
  - Hypotonia with history of poor suck; **OR**
- Individual is between 6 through 12 years of age with the following characteristics:
  - Excessive eating with central obesity if uncontrolled; **AND**
  - GDD as defined by the presence of delay in at least 2 developmental domains*****; **AND**
  - History or presence of hypotonia with poor suck; **OR**
- Individual is 13 years of age or older with the following characteristics:
  - Excessive eating with central obesity if uncontrolled; **AND**
  - Hypothalamic hypogonadism; **AND**
  - Intellectual disability as defined by the presence of impaired intellectual and adaptive functioning in at least 1 adaptive domain

*****Developmental domains are gross/fine motor, speech/language, cognition, social/personal and activities of daily living[2]

**PWS Testing Strategy:**
- Testing begins with DNA methylation analysis of the 15q11.2 – q13 chromosome region (eg, *SNRPN* gene)
  - If DNA methylation analysis is pathogenic or a likely pathogenic variant is identified, then proceed to FISH or CMA
    - If FISH or CMA is normal, then proceed to UPD study
    - If UPD is normal, then proceed to ID study

## Coverage Limitations

Humana members may **NOT** be eligible under the Plan for **genetic testing for AS or PWS** for any indications other than those listed above. This is considered experimental/investigational as it is not identified as

widely used and generally accepted for any other proposed use as reported in nationally recognized peer-reviewed medical literature published in the English language.

## Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

| CPT® Code(s) | Description | Comments |
|---|---|---|
| 81331 | SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (eg, Prader-Willi syndrome and/or Angelman syndrome), methylation analysis | |
| 96040 | Medical genetics and genetic counseling services, each 30 minutes face-to-face with patient/family | |
| **CPT® Category III Code(s)** | **Description** | **Comments** |
| No code(s) identified | | |
| **HCPCS Code(s)** | **Description** | **Comments** |
| S0265 | Genetic counseling, under physician supervision, each 15 minutes | |

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## Appendix

**Appendix A**
**Pre- and Post-Test Genetic Counseling Criteria**

| **Pre- and post-test genetic counseling performed by any of the following qualified medical professionals** |
|---|
| Genetic counselor who is board-certified or board-eligible by the American Board of Medical Genetics and Genomics (ABMGG) or American Board of Genetic Counseling, Inc (ABGC) and is not employed by a commercial genetic testing laboratory; **OR** |
| Genetic clinical nurse (GCN) or advanced practice nurse in genetics (APNG) who is credentialed by the Genetic Nursing Credentialing Commission (GNCC) or the American of Nurses Credentialing Center (ANCC) and is not employed by a commercial genetic testing laboratory; **OR** |
| Medical geneticist who is board-certified or board-eligible by ABMGG; **OR** |
| Treating physician who has evaluated the individual to be tested and has completed a family history of three generations |

**Appendix B**
**Adaptive Skills Used to Define and Determine Intellectual Disability[15]**

| Adaptive Domain | Skills |
|---|---|
| Conceptual | These skills include language, reading and writing (literacy); money, time and number concepts (mathematics); reasoning; memory; self-direction; and judgment in novel situations. |
| Social | These skills include interpersonal social communication, empathy and ability to relate to peers as friends, social problem-solving, social responsibility and self-esteem. Gullibility, the ability to follow rules and avoiding victimization may also be included. |
| Practical | These skills include activities of personal care or daily living, such as eating, dressing, mobility and toileting. Additional skills may include following a schedule or routine, using a telephone, managing money, preparing meals, occupational skills and abilities in transportation/ travel, health care and safety. |

## Change Summary

- 04/25/2024 Annual Review, No Coverage Change.