**XomeDx Medical Necessity Attestation Form**
**Texas Health Steps Comprehensive Care Program (EPSDT)**
**Whole exome sequencing (CPT 81415, 81416)**

| | |
|---|---|
| **Date** | |
| **Patient name** | |
| **Date of birth** | |
| **Medicaid plan & ID number** | |

Coverage is requested for whole exome sequencing (WES) for this Medicaid beneficiary under the Texas Health Steps Comprehensive Care Program. WES meets the definition of medical necessity for this beneficiary under 25 Texas Admin. Code § 33.2 (8).

Texas SB989, effective 9/1/23, mandates the coverage of biomarker tests such as WES under 8 Texas Insurance Code Subtitle E, Chapter 1372, for the purpose of diagnosis and appropriate management of a disease or condition to guide treatment when the test is supported by medical and scientific evidence and/or nationally recognized clinical practice guidelines.

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**I certify that the requested diagnostic service is medically necessary, as defined by Tex. Admin. Code, and the following are true:**

- ☑ The patient is under age 21
- ☑ The patient has undergone informed consent and counseling with a specialist with expertise in the conditions and/or relevant genes for which testing is being considered
- ☑ The patient's clinical presentation does not fit a well-described syndrome for which single-gene or single targeted panel test is available, but genetic etiology is the likely explanation
- ☑ The patient's clinical presentation is consistent with indications for which WES is recommended by professional society guidelines and/or peer-reviewed, published literature
- ☑ WES is more efficient or economical than the separate single-gene tests or panels that would be recommended based on the differential diagnosis.
- ☑ WES test results are expected to directly influence clinical decision-making and/or clinical outcome as follows:

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_____ _____

Ordering provider signature
(or authorized representative)

Ordering provider printed name
(or authorized representative)

GeneDx

**Background on whole exome sequencing:**

Most known genetic mutations that cause human disease occur in exons, which are individual pieces of DNA that provide instructions for making proteins. These protein-making pieces of DNA are collectively called the exome and comprise less than 2% of the human genome. Whole exome sequencing (WES) is a highly efficient diagnostic test that identifies variations in the exons of all genes, rather than testing only one or a few genes at a time.[1]

WES has been available as a clinical diagnostic tool since 2011 and, over the past decade, WES has increasingly been used as the single genetic test which can provide a timely diagnosis to inform appropriate care. Major insurers, including UnitedHealthcare, Cigna, and BCBS Texas, have covered WES since 2016 for patients with neurodevelopmental disorders suspected to be genetic in nature.[2] Today, over 90% of commercially insured lives in the US and Medicaid beneficiaries in 28 states have coverage for WES for suspected genetic disease when the clinical presentation is nonspecific and does not fit a well-defined syndrome for which a specific or targeted gene test is available.

In addition, professional society guidelines from the American College of Medical Genetics and Genomics (ACMG), the National Society of Genetic Counselors (NSGC), and the American Epilepsy Society (AES) all support the use of WES as a first-line diagnostic test for a variety of indications.

**Medical necessity as defined by 25 Tex. Admin. Code § 33.2 (8):**

The Texas Health Steps definition of medical necessity is established in 25 Tex. Admin. Code § 33.2 (8) and is composed of the six criteria below (paragraphs A through F). The following demonstrate the medical necessity of the requested service in alignment with the published criteria:

**A** ***Reasonable and necessary to prevent illness, medical or dental conditions, or provide early screening, interventions, and/or treatments for conditions that cause suffering or pain, cause physical deformity or limitations in function, threaten to cause, or worsen a disability, cause illness or infirmity of a client, or endanger life.***

WES is both reasonable and necessary for diagnosing this patient. Establishing a diagnosis based on clinical signs and symptoms is often challenging given the genetic and phenotypic heterogeneity associated with rare genetic disease. This patient's clinical presentation is nonspecific and does not fit a well-defined syndrome for which a specific or targeted gene test is available.

Previous standard of care tests, including CMA, single gene, and multi-gene panel tests, provided substantially lower diagnostic yields and clinical utility at a typically much higher cumulative cost. Utilizing tests other than WES would only serve to extend the diagnostic odyssey, thereby delaying diagnosis and optimal treatment for this patient. Denying coverage for this test may expose the patient to ineffective therapies, irreversible deterioration of their condition, and unnecessary iterative testing and procedures.[4]

**B** ***Consistent with health care practice guidelines and standards that are issued by professionally recognized health care organizations or governmental agencies.***

The use of WES is supported by the evidence-based clinical practice guidelines of the American College of Medical Genetics and Genomics (ACMG), the National Society of Genetic Counselors (NSGC), and the American Epilepsy Society (AES).

1. MedlinePlus, National Library of Medicine, July 28, 2021.
2. Douglas MP, Parker SL, Trosman JR, Slavotinek AM, Phillips KA. Private payer coverage policies for exome sequencing (ES) in pediatric patients: trends over time and analysis of evidence cited. Genet Med. 2019 Jan;21(1):152-160. doi: 10.1038/s41436-018-0043-3. Epub 2018 Jul 12. PMID: 29997388; PMCID: PMC6329652.
3. Policy Reporter, 2023

The American College of Medical Genetics and Genomics (ACMG) published evidence-based guidelines strongly recommending whole exome or genome (WGS) for patients with (a) one or more congenital anomalies (CA) with onset before age one year or (b) developmental delays (DD) or intellectual disability (ID) with onset before age 18 years in the peer-reviewed medical journal Genetics in Medicine on July 1, 2021.[4] This guideline is based on a comprehensive systematic review of published evidence, including an analytic framework for evaluating outcomes of WES for patients with CA/DD/ID.[5]

In October 2022, the National Society of Genetic Counselors (NSGC) released an evidence-based guideline strongly recommending WES as a first-tier test for individuals with unexplained epilepsy regardless of age. This guideline was based on a systematic evidence review of peer-reviewed literature which included 40 studies with over 3,000 patients who had ES and demonstrated a genetic diagnosis led to changes in clinical management.[6] Additionally, the guideline discussed that expanding access to genetic testing may "lead to a decrease in existing health disparities;" but acknowledged insurance reimbursement remains a barrier.[7] Notably, the NSGC guideline was endorsed by the American Epilepsy Society (AES) in Sept 2022.

The ACMG 2021 Guidelines and the NSGC 2022 Guidelines powerfully demonstrate the medical necessity and clinical utility of WES in clinical scenarios like that of this patient. These guidelines are available for review online:

**ACMG 2021: https://www.gimjournal.org/article/S1098-3600(21)05168-6/fulltext**
**NSGC 2022: https://onlinelibrary.wiley.com/doi/10.1002/jgc4.1646**

**C** ***Consistent with the diagnoses of the conditions.***

As discussed in the ACMG 2021 and NSGC 2022 Guidelines:

• WES is proven, accepted, and widely used by physicians when a genetic condition is suspected, and the patient's clinical presentation is nonspecific and does not fit a well-defined syndrome for which a specific or targeted gene test is available. - ACMG

• Identifying an underlying diagnosis for CA/DD/ID through WES "can lead to changes in management that will influence mortality, morbidity, and reduce the burden on patients and families…" - ACMG

• "Many genetic epilepsy syndromes have been described, and a majority of otherwise unexplained epilepsy, that which cannot be attributed to an acquired etiology such as trauma, infection or stroke, is now assumed to have an underlying genetic etiology." - NSGC

• Increased use of WES "has uncovered the broader spectrum of disease associated with genetic variants and further increased diagnostic yield leading to improved patient outcomes." This is not possible using standard genetic tests such as CMA and panel tests which commonly miss disease-causing variants identified using sequencing technology. - ACMG

4. Manickam, K., McClain, M.R., Demmer, L.A. et al. Exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability: an evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). Genet Med 23, 2029–2037 (2021). https://doi.org/10.1038/s41436-021-01242-6
5. Malinowski, J., Miller, D.T., Demmer, L. et al. Systematic evidence-based review: outcomes from exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability. Genet Med 22, 986–1004 (2020). https://doi.org/10.1038/s41436-020-0771-z
6. Sheidley, B. R., Malinowski, J., Bergner, A. L., Bier, L., Gloss, D. S., Mu, W., Mulhern, M. M., Partack, E. J., & Poduri, A. (2022). Genetic testing for the epilepsies: A systematic review. Epilepsia, 63(2), 375-387. https://doi.org/10.1111/epi.17141
7. Smith, L., Malinowski, J., Ceulemans, S., Peck, K., Walton, N., Sheidley, B. R., & Lippa, N. (2022). Genetic testing and counseling for the unexplained epilepsies: An evidence-based practice guideline of the National Society of Genetic Counselors. J Genet Couns. https://doi.org/10.1002/jgc4.1646

**D** ***No more intrusive or restrictive than necessary to provide a proper balance of safety, effectiveness, and efficiency.***

WES is widely accepted as a safe, effective, and efficient diagnostic test and is now strongly recommended as a first-tier diagnostic (see ACMG 2021 Guidelines, NSGC 2022 Guidelines). Single gene and panel tests are no longer recommended for first-tier testing, except when the physician reasonably suspects a specific genetic cause and needs confirmation. As previously mentioned, that is not the case with this patient.

Alternatives to WES – such as CMA and multi-gene panel tests – have a low rate of diagnosis and only serve to unnecessarily delay diagnosis and treatment, extend the diagnostic odyssey, and expose the child to further pain and discomfort. Compared to WES, the alternative tests are highly inefficient, with lower clinical utility.

**E** ***Not experimental or investigative.***

There is ample evidence that WES, as requested, is <u>not</u> experimental or investigational.

• This authorization request is consistent with published evidence-based professional society guidance from multiple organizations, including ACMG 2021 Guidelines and NSGC 2022 Guidelines.

• WES has been available as a clinical diagnostic tool in the US since 2011 and has become standard of care in rare disease diagnosis. Major insurers, including UnitedHealthcare, Cigna, Aetna, and BCBS have covered WES since 2016 for patients with neurodevelopmental disorders suspected to be genetic in nature.2 Today, over 90% of commercially insured lives in the US and Medicaid beneficiaries in 28 states have coverage for WES for suspected genetic disease when the clinical presentation is nonspecific and does not fit a well-defined syndrome for which a specific or targeted gene test is available.3 Broad payer coverage further demonstrates WES is not experimental or investigational.

**F** ***Not primarily for the convenience of the client or provider.***

The requested WES test is, by its nature, purpose, and use, not for the convenience (primarily or otherwise) of the patient or provider. The requested WES test is necessary to:
• Determine clinical diagnosis(es)
• Identify the gene(s) implicated in the child's genetic condition(s)
• Identify appropriate treatment
• Guide clinical care management

**Texas Biomarker Law (SB989), effective Sept 1 2023**

Texas SB989, effective 9/1/23, mandates the coverage of biomarker tests such as WES under 8 Texas Insurance Code Subtitle E, Chapter 1372, for the purpose of diagnosis and appropriate management of a disease or condition to guide treatment when use of the test is supported by medical and scientific evidence and/or nationally recognized clinical practice guidelines. As established in this document, evidence-based clinical practice guidelines support the use of WES for this patient's clinical profile.