XomeDX® Medical Necessity Attestation Form
The Alabama EPSDT Program
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 Alabama Early and Periodic Screening, Diagnostic and Treatment (EPSDT) program. WES meets the Alabama Medicaid definition of medical necessity for this beneficiary, as defined by Alabama State Administrative code 560-x-11-.14.

I certify that the requested diagnostic service is medically necessary, as defined by the Alabama EPSDT Program, is being ordered in accordance with generally accepted standards of medical practice, 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:

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. 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.[3]

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 Alabama State Administrative Code 560-x-11-.14:

The following outlines the medical necessity of whole exome sequencing in alignment with the Alabama EPSDT Program definition of medical necessity:

Alabama definition of medical necessity:

"Medically necessary service" means any health care service, intervention, or supply (collectively referred to as "service") that a physician (or psychologist, when applicable), exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing, or treating an illness, [including mental illnesses and substance use disorders], injury, disease, condition, or its symptoms, in a manner that is:

- in accordance with generally accepted standards of medical practice;
- clinically appropriate in terms of type, frequency, extent, site and duration, and considered effective for the patient's illness, injury, disease, or condition;
- in accordance with medical necessity "guidelines/references" in Agency's Administrative Code, State Plan, and Provider Manual;
- not primarily for the convenience of the patient or provider;
- not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury, disease, or condition.
- the service is not contraindicated; and
- the provider's records include sufficient documentation to justify the service.

For these purposes, "generally accepted standards of medical practice" means:

- Standards that are based on credible scientific evidence published in peer reviewed medical literature generally recognized by the relevant medical community are required when applicable; or
- Alternatively, may consider physician specialty society recommendations [clinical treatment guidelines/guidance] and/or the general consensus of physicians practicing in relevant clinical areas.

WES is required for the care and well-being of this patient and is being ordered within generally accepted standards of medical or professional practice. 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. Without a definitive diagnosis, this patient's care team cannot develop an optimal treatment plan. Earlier diagnosis and interventions provide improved outcomes and can avoid loss of function for many neurodevelopmental disorders.

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]

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).

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

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 80% 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 that the medical necessity of WES is well established and is the standard of care.

References: 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. **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 systema ic 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 .