**Letter of Medical Necessity for Rapid Genome Sequencing (Proband)**

**Patient Information**

**Date:**

**Patient Name:**

**Patient DOB:**

**Insurance Company Name, Address, City, State:**

**Policy Number:**

**Group Number:**

**ICD10 Codes:**

**Test Information**

**Test Name:** Genome*Xpress* - Proband

**CPT Codes:** 81425x1

**Laboratory:**

GeneDx, Inc.

(NPI#1487632998 / TAXID#205446298 / CLIA#21D0969951)

207 Perry Parkway

Gaithersburg, MD 20877

Telephone: (301) 519-2100

Fax: (201) 421-2010

This letter is regarding my patient, [FIRST NAME LAST NAME], to request full coverage for the Genome*Xpress-*Probandfor rapid genome sequencing (rGS) to be performed by GeneDx. It is my professional determination that testing is medically necessary and will have a direct impact on this patient’s treatment and management. I have included relevant information for my patient as well as summaries of the published peer-reviewed evidence and clinical guidelines that support this testing.

**Patient Clinical and Family History and Potential Impact of Test Results**

This testing is requested due to this patient’s personal medical history, which includes the following clinical findings:

* Add Relevant Phenotype
* Add Relevant Phenotype
* Add Relevant Phenotype

The patient’s family history is negative for related conditions / unknown / remarkable for the following related clinical features:

The patient has previously had the following uninformative genetic and other testing:

* Add test
* Add test
* Add test

Due to this history, the differential diagnosis includes (list at least 3 conditions you are considering for this patient).

Specifically for my patient, results of rGS will guide prognosis and improve clinical decision-making which can improve clinical outcomes by: (keep all bullets you think are relevant and provide examples/details for each included)

* change in medication: (provide examples of potential new treatments or halting of existing ones that may be recommended based results)
* alteration to diet: (provide examples of potential alteration to diet that may be recommended based results)
* change in planned procedures or surveillance: (provide examples of potential alteration surgery, imaging, and/or diagnostic studies that may be recommended based on results especially state if includes discontinuation of unnecessary procedures)
* Impact on future reproductive planning by informing genetic counseling related to recurrence risk and prenatal diagnosis options: (include and provide additional details if patient’s first degree relative is pregnant or considering pregnancy)

**Clinical Evidence and Guidelines for Testing**

More than 20 studies have reported diagnostic rates of rGS in critically ill infants and children.1 Studies report a diagnostic yield in the range of ~40% to 50% for rGS2-4 and a diagnostic yield of rGS at least two times greater than traditional testing (e.g. chromosomal microarray and multigene panel testing).3

Prominent professional societies including the American College of Genetics and Genomics (ACMG) have published evidence-based guidelines strongly recommending genome sequencing (GS) as a first-tier test.5

**Rapid Genome Sequencing Leads to Changes in Medical Management**

Clinical utility studies have reported approximately a 40% to 60% change in medical management for individuals with a positive rGS result. These modifications included change in medication (new treatment or halting an existing one), alteration to diet, change in planned procedures or surveillance (surgery, imaging, and/or diagnostic studies), and/or impact on future reproductive planning. Some of these changes included preventing the need for expensive and/or invasive testing or surgical procedures, discontinuing ineffective medications, or withdrawal of care/start of palliative care.2-4,6-8 In a United States based study, management changes based on rGS results prevented morbidity in over 50% of the diagnosed infants compared to no infants who had traditional testing.3

**Summary**

Genome*Xpress-*Probandis a highly sensitive and cost-effective genetic test. I am requesting coverage for this medically necessary test to establish appropriate medical management for this patient. Without testing, treatment would be suboptimal, subjecting this patient to increased morbidity and potentially early mortality.

Thank you for your review and consideration. If you have questions, or if I can be of further assistance, please do not hesitate to call me at (XXX) XXX-XXXX.

Sincerely,

Signature

Ordering Provider’s Name

References

1. Stark, Z. and S. Ellard, Rapid genomic testing for critically ill children: time to become standard of care? Eur J Hum Genet, 2022. 30(2): p. 142-149.

2. Dimmock, D., et al., Project Baby Bear: Rapid precision care incorporating rWGS in 5 California children's hospitals demonstrates improved clinical outcomes and reduced costs of care. Am J Hum Genet, 2021. 108(7): p. 1231-1238.

3. Farnaes, L., et al., Rapid whole-genome sequencing decreases infant morbidity and cost of hospitalization. NPJ Genom Med, 2018. 3: p. 10.

4. Sanford, E.F., et al., Rapid Whole Genome Sequencing Has Clinical Utility in Children in the PICU. Pediatr Crit Care Med, 2019. 20(11): p. 1007-1020.

5. Manickam, K., 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, 2021. 23(11): p. 2029-2037.

6. D'Gama, A.M., et al., Evaluation of the feasibility, diagnostic yield, and clinical utility of rapid genome sequencing in infantile epilepsy (Gene-STEPS): an international, multicentre, pilot cohort study. Lancet Neurol, 2023. 22(9): p. 812-825.

7. French, C.E., et al., Whole genome sequencing reveals that genetic conditions are frequent in intensively ill children. Intensive Care Med, 2019. 45(5): p. 627-636.

8. Lunke, S., et al., Integrated multi-omics for rapid rare disease diagnosis on a national scale. Nat Med, 2023.