# LETTER OF MEDICAL NECESSITY FOR EXOME SEQUENCING

**(ExomeNext-Proband, Duo and Trio)**

Date: Date of service/claim

To: Utilization Review Department

Insurance Company Name, Address, City, State

Re: Patient Name, DOB, ID #

Commonly Used ICD-10 Codes: (Quick reference guide – provider is responsible for selecting most appropriate code(s) based on individual assessment of the patient)

Code Description

F84.0 AUTISTIC DISORDER

F88 OTHER DISORDERS OF PSYCHOLOGICAL DEVELOPMENT Q89.7 MULTIPLE CONGENITAL ANOMALIES

P94.2 NEONATAL HYPOTONIA G40.909 EPILEPSY, UNSPECIFED

H90.3 SENSORINEURAL HEARING LOSS, BILATERAL

R62.50 UNSPECIFIED LACK OF EXPECTED NORMAL PHYSIOLOGICAL DEVELOPMENT IN CHILDHOOD F79 INTELLECTUAL DISABILITY

Q02 MICROCEPHALY

Q18.9 DYSMORPHIC FACIAL FEATURES

This letter is regarding my patient and your subscriber, referenced above, requesting full coverage of medically indicated genetic testing for exome sequencing to be performed by Ambry Genetics Corporation.

Exome sequencing analyzes the set of protein-coding regions of the human genome. Approximately 85% of genetic changes that cause known diseases occur within exomes.1 Although not required, testing of additional family members (usually parents and/or siblings) along with the patient/proband, referred to as duo or trio testing, can add additional comparative information that is helpful in reaching a genetic diagnosis. Whole exome sequencing has been shown to be highly effective for diagnosing individuals with previously unidentified genetic conditions.2,7,8

The American College of Medical Genetics and Genomics (ACMG) 2012 Policy Statement on genomic sequencing3

# recommends exome sequencing for the following clinical scenarios:

* The patient’s clinical presentation (phenotype) and family history strongly implicate a genetic etiology, but phenotype does not correspond with a specific disorder for which a clinical targeted genetic test is available
* Clinical presentation (including fetal, with limitations) suggests a likely genetic disorder, but specific genetic tests (including targeted sequencing tests) for phenotype have failed to provide a diagnosis
* A defined genetic disorder with a high degree of genetic heterogeneity is suspected, making whole exome or genome sequencing of multiple genes simultaneously a more practical approach

More recently, the ACMG 2021 clinical guideline on genomic sequencing4 **strongly recommends exome sequencing as a first- or second-tier test for pediatric patients with:**

* One or more congenital anomalies diagnosed prior to one year of age;
* Developmental delay or intellectual disability with onset prior to 18 yo.

Additionally, as of July 2025, the American Academy of Pediatrics also recommend whole exome or whole genome sequencing as a first-tier test for **global developmental delay (GDD)/intellectual disability (ID)** due to its higher diagnostic yield and greater cost-effectiveness when performed early in the evaluation process.5 The reported diagnostic yield of whole exome sequencing in these cases ranges from 28% to 43%. A genetic diagnosis for individuals with GDD/ID allows for accurate prognostication, supports monitoring for associated complications, informs recurrence risk for patients and their family members, and in some cases, can directly impact treatment or identify individuals as candidates for future treatments. A genetic diagnosis may also reduce further unnecessary diagnostic testing and/or invasive procedures, and allow access to developmental therapies/services, appropriate disease-specific support networks, or clinical trials.5

# Significant aspects of my patient’s medical and/or family history that raise suspicion of an underlying genetic diagnosis are as follows: [check all that apply]

 Biochemical findings suggestive of an inborn error of metabolism

 Congenital anomalies affecting more than one unrelated organ systems

 Congenital anomaly affecting a single organ system

 Developmental delay/intellectual disability

 Autism spectrum disorder

 Developmental regression that is unexplained

 Complex neurodevelopmental or severe neuropsychiatric condition

 Family history is strongly suggestive of a genetic etiology, including consanguinity

**Previous testing has failed to identify a diagnosis in my patient.** Due to the heterogeneous nature of my patient’s symptoms and the uninformative test results thus far, per ACMG guidelines exome sequencing is warranted for my patient.3,4

# Clinical exome sequencing has a significant likelihood of providing my patient and family with an accurate diagnosis 6. This, in turn, can lead to:

* Specific treatment or management strategies that can dramatically change the clinical outcome.2,7,8
* Identification of necessary medical referrals, screening for associated complications, and recurrence risk counseling.2,7,8
* Decreased medical costs due to ending the diagnostic odyssey.2,7

**As such, I am ordering this medically necessary test and affirm that my patient has provided informed consent for genetic testing.** I recommend that you support this request for coverage of exome sequencing in my patient.

Thank you for your time and please don’t hesitate to contact me with any questions. Sincerely,

Ordering Clinician Name (Signature Provided on Test Requisition Form)

(MD/DO, Clinical Nurse Specialist, Nurse-Midwives, Nurse Practitioner, Physician Assistant, Genetic Counselor\*)

\*Authorized clinician requirements vary by state