I. Policy: Whole Exome Sequencing

II. Purpose/Objective:
To provide a policy of coverage regarding whole exome sequencing

III. Responsibility:
A. Medical Directors
B. Medical Management

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards of good medical treatment practiced by the general medical community.
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment
Medical Necessity shall mean a service or benefit that is compensable under the Medical Assistance Program and if it meets any one of the following standards:

(i) The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition or disability.
(ii) The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental or development effects of an illness, condition, injury or disability.
(iii) The service or benefit will assist the Member to achieve or maintain maximum functional
capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for members of the same age.

DESCRIPTION:
Whole exome sequencing is a strategy to selectively sequence the coding regions of the genome. Exons are short, functionally important sequences of DNA which represent the coding regions of genes. In the human genome there are about 180,000 exons which represents about 1% of the human genome. The goal of this approach is to focus on the 1% of the genome that corresponds to functional variation responsible for both Mendelian and common diseases, rather than examining DNA sequence from the whole genome, the majority of which has not yet been linked to clinically relevant information.

INDICATIONS: REQUIRES PRIOR AUTHORIZATION by a Plan Medical Director or Designee
Whole exome sequencing will be considered for coverage when used for the evaluation of exonic sequence changes in children when all of the following criteria are met:

1. Test is ordered by one of the following provider types:
   - Medical Geneticist
   - Licensed and/or Certified Genetic Counselor
   - Neurologist
   - Developmental Pediatrician

2. The child (defined as under the age of 21) exhibits at least one of the following:
   - Autism spectrum disorder;
   - Non-syndromic developmental delay, loss of developmental milestones, or intellectual disability
   - Congenital anomalies, malformation(s), or dysmorphic features not specific to a well delineated genetic syndrome
   - Suspected Mendelian condition in which multiple genes could potentially account for the phenotype
   - Complex epilepsy, including drug resistant epilepsy or epileptic encephalopathy

3. Clinically indicated testing (e.g., fragile X, metabolic, etc) has not been diagnostic; and

4. The genetic testing results have reasonable potential to impact the clinical management and/or preventive surveillance strategies; and

5. The parents/legal guardians have been appropriately counseled about the testing by a qualified professional (same or similar to ordering providers) who is involved in the child’s care

EXCLUSIONS: The Plan does NOT provide coverage for the use of whole exome sequencing for indications other than those listed above because it is considered experimental, investigational or unproven. There is currently insufficient evidence in the peer-reviewed published medical literature to establish the effectiveness of this modality on health outcomes when compared to established tests or technologies.

Note: A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in MP 15 - Experimental Investigational or Unproven Services or Treatment.

CODING ASSOCIATED WITH:
The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services.

81415 Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis
81416 Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (eg parents, siblings)
81417 Exome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained exome sequence (eg, updated knowledge or unrelated condition/syndrome)
LINE OF BUSINESS:
Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supersede this policy. For PA Medicaid Business segment, this policy applies as written.

REFERENCES:
Feldman L. Managing the cost of diagnosis. Managed Care 2009 May, p 43-45.
Biesecker LG, Green RC. Diagnostic clinical genome and exome sequencing. NEJM 2014;370:4218-4225.
Hayes GTE Report. Whole Exome Sequencing for Cancer Indications. Reviewed July 1, 2014
Taylor JC, Martin HC, et al. factors influencing success of clinical genome sequencing across a broad spectrum of disorders. Nature Genetics 2015 May 18. Doi: 10.1038/ng.3304


This policy will be revised as necessary and reviewed no less than annually.

Devised: 1/14
Revised: 1/16 (added indications)
Reviewed: 2/15, 2/17