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Sent: Friday, December 22, 2023 12:17 PM
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Cc: Alka Chaubey <achaubey@bionano.com>; Justin Leighton <jleighton@bionano.com>; Annemarie Benton <abenton@bionano.com>
Subject: [EXTERNAL] New LCD Request LCD - MolDX: Optical Genome Mapping (OGM) Lab-Developed test for Hematological Malignancies and Suspected Hematological Malignancies

Dear MolDx team,

On behalf of Bionano Laboratories, please accept this request for coverage of the OGM-Dx™ HemeOne™.

As we discussed during our March 29th conference call, the **OGM-Dx™ HemeOne™** test is intended to be used as a replacement for the cytogenetic methods that have been used to identify structural variants in hematological malignancies by Bionano Laboratories.

The analytic validity, clinical validity and utility of the test have been demonstrated in multiple peer-reviewed articles. The test is performed in Bionano Laboratories, a CLIA registered clinical laboratory which is CAP accredited.

You can find a copy of all the documents below:

1. Dossier with Executive Summary for OGM-Dx™ HemeOne™.
2. Laboratory Validation report for OGM-Dx™ HemeOne™.
3. Full PDFs of key publications
4. OGM-Dx™ HemeOne™. Test Requisition Form (TRF)in dossier
5. OGM-Dx™ HemeOne™. Sample Reports within the dossier

New LCD Request Submission Criteria (Required)
A complete request must:

- Clearly identify the statutorily-defined Medicare benefit category to which the requestor believes the item or service falls under and provide a rationale justifying the assignment;

This is a request for a Part B medically necessary clinical laboratory test for patients with a hematological malignancy or suspected of having one. *Reference section of the SSA "Under §1861(s)(3) diagnostic laboratory tests, and other diagnostic tests"*

- Identify the language that the requestor wants in a new LCD

Criteria for Coverage

-Testing is performed on bone marrow biopsies, bone marrow aspirates, bone marrow clots, peripheral blood samples, or extramedullary sites suspected of harboring a hematological malignancy (myeloid or lymphoid).
-For patients that do not have a diagnosis of a hematological malignancy, where one is suspected, the patient must have an undefined persistent cytopenia (not otherwise specified), and other possible causes have been reasonably excluded.
Optical Genome Mapping (OGM) will be considered reasonable and necessary in the evaluation of biological specimens (mentioned above) in the following clinical circumstances:

- Newly diagnosed patients or patients with clinical suspicion of hematological malignancies (e.g. who are suitable candidates for post-induction transplantation or consolidation therapy or targeted therapy or suitable candidates for clinical trials at the time of testing, and meet one of the following cytogenetic criteria:
    - normal or abnormal genome
- Previously diagnosed patients with hematological malignancies who have not responded to induction chemotherapy, or who have progressed following induction.
- Patients with hematological malignancies, who have responded to treatment, either chemotherapy or transplantation, with evidence of relapse.

Limitations

- Specimen types that are not compatible with OGM such as lymph node biopsies.
- Specimens that do not meet the minimum criteria of 1.5 million cells
- Not suitable for Minimal Residual Disease (MRD).

Include a justification for the new LCD supported by peer-reviewed evidence. Full-text copies (not abstracts or meeting poster presentations) of published evidence from peer-reviewed literature must accompany the request. Failure to include full-text clinical literature invalidates the request;

The above link contains the full key publications for OGM in hematological malignancies.

- Include information that addresses the relevance, usefulness, clinical health outcomes, or the medical benefits of the item or service;

An excerpt from the attached documentation is provided here-

> Comprehensive identification of structural chromosomal aberrations (also known as structural variations (SVs)) is crucial for the evaluation of hematological malignancy samples for accurate classification and risk stratification of cases. Many SVs are missed when relying on widely used traditional cytogenetic methods, such as karyotyping (KT), fluorescence *in situ* hybridization (FISH), and chromosomal microarray (CMA).
>
> Optical Genome Mapping (OGM) has been proven as a technique that can maximize the detection of all classes of structural variations or chromosomal aberrations. Numerous scientific studies have demonstrated that OGM not only provides results that correlate to findings from traditional cytogenetics modalities but that it also reveals more pathogenic variants of clinical relevance.

- Include information that fully explains the design, purpose, and/or method, as appropriate, of using the item or service for which the request is made

- *An excerpt from the attached documentation is provided here-*
    1. Optical Genome Mapping (OGM) analyzes the fluorescent labeling patterns of DNA at the molecular level to identify genome-wide structural variants (insertions, deletions, duplications, inversions, translocations), and complex rearrangements with a resolution down to approximately 5000 base pairs (bp) at low variant allele fraction. The resolution provided by OGM far exceeds that of conventional cytogenic modalities without the need for DNA sequence level information.
    2. OGM relies on the extraction and analysis of Ultra-High Molecular Weight (UHMW) DNA. DNA is fluorescently labeled via covalent modification at CTTAAG hexamer motifs, generating a genome-wide density of approximately 14-17 labels per 100 kbp in sequence specific patterns. Labeled DNA is loaded on silicon chips comprised of approximately 100,000 parallel nanochannels where individual DNA molecules are linearized, imaged, and digitized thus creating a DNA "barcode". This high resolution DNA labeling banding pattern (profile) is then utilized to detect copy number variations (CNVs) and structural variations (SVs) with high sensitivity and specificity through comparison to a human refence genome database (comprised of hundreds of healthy individuals).

Thank you for your consideration, and please let me know if you have any questions,

Donna

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