

LCD for Flow Cytometry (L30161)

Contractor Information

Contractor Name

Wisconsin Physicians Service Insurance Corporation

Contractor Number

00951, 00952, 00953, 00954, 52280, 05101, 05201, 05301, 05401, 05102, 05202, 05302, 05402

Contractor Type

Carrier – MAC – FI

LCD Information

LCD ID Number

L30161

LCD Title

Flow Cytometry

Contractor's Determination Number

PATH-016

AMA CPT / ADA CDT Copyright Statement

CPT codes, descriptions and other data only are copyright 2009 American Medical Association (or such other date of publication of CPT). All Rights Reserved. Applicable FARS/DFARS Clauses Apply. Current Dental Terminology, (CDT) (including procedure codes, nomenclature, descriptors and other data contained therein) is copyright by the American Dental Association. © 2002, 2004 American Dental Association. All rights reserved. Applicable FARS/DFARS apply.

CMS National Coverage Policy

CMS National Coverage Policy

Title XVIII of the Social Security Act section 1862 (a)(1)(A). This section allows coverage and payment of those services that are considered to be medically reasonable and necessary.

Title XVIII of the Social Security Act section 1862 (a)(7). This section excludes routine physical examinations and services

Title XVIII of the Social Security Act section 1833 (e). This section prohibits Medicare payment for any claim which lacks the necessary information to process the claim.

Oversight Region

Region V

Original Determination Effective Date

For services performed on or after 11/16/2009

Original Determination Ending Date**Revision Effective Date**

For services performed on or after 11/16/2009

Revision Ending Date**Indications and Limitations of Coverage and/or Medical Necessity****Indications and Limitations of Coverage and/or Medical Necessity**

Flow Cytometry is a cell analysis process performed by allowing cells in liquid suspension to pass through a laser-produced beam of light for the actual analysis of the cell. Specimens are usually treated with reagents that are chosen to amplify certain signals, such as antigens on a cell surface or within the cytoplasm or nucleus, or DNA content within a cell. Data is generated and organized by the instrument. Clinical analysis and interpretations are performed by an experienced physician, usually a hematopathologist.

A. Immunophenotyping:

The cells of the immune system bear on their surfaces and within their cytoplasm or nucleus hundreds of molecules specific for their particular developmental stage and functional state. There have been more than 260 types of molecules identified on the surface of human leukocytes but only around 30 of these are associated with a known structure or function.

The process of measuring the types of antigens expressed on and within a cell by flow cytometry is referred to as immunophenotyping. To detect these antigens, antigen-specific monoclonal antibodies are used which have been labeled with a fluorescent dye or fluorochrome. After washing away any unbound antibody, the cells are analyzed by flow cytometry which categorizes them by size, granularity and fluorochrome intensity. An international standard nomenclature is used to categorize most antibodies according to the antigens they detect. Each category is called a cluster of differentiation (CD) and is numbered. A few clinically useful antibodies have not yet been "clustered" and are referred to by names derived from site of origin or nomenclature used in other classification systems (e.g. histocompatibility and immunoglobulin antigens).

DNA content (ploidy) and cell proliferative activity (S-phase fraction or %S-phase)

1. Malignant cells sometimes show abnormalities in total chromosome number and the frequency of these abnormalities generally increases with progression to higher-grade tumors.

Flow cytometric methods can be used to measure nuclear deoxyribonucleic acid (DNA) content (ploidy) as a prognostic indicator of solid tumors. Fluorescent dyes are used to stain nucleic acids.

DNA diploid tumors are those where a single peak containing an amount of DNA similar to normal cells is generated by flow cytometry. DNA aneuploid tumors have additional peaks on the DNA histogram which may represent cells containing more or less nucleic acid found in 46 normal chromosomes.

A more quantitative method of expression is the DNA index (DI), which is the ratio of the mean tumor sample G0/G1 DNA content divided by the mean G0/G1 DNA content of normal diploid reference cells. The greater the deviation of the DI from 1, the more "aneuploid" the tumor.

2. The assessment of % S-phase or the S phase fraction (SPF) measures the percentage or proportion of cells preparing for mitosis by their active doubling of DNA. Tumor cells tend to replicate more readily than normal cells therefore increased SPF activity can raise the question of malignancy. Frequently a high SPF will correlate positively with poor differentiation, increasing tumor size and degree of aggressiveness.

A. Immunophenotyping (88184-88189) is indicated for the following conditions:

1. Leukemia or Lymphoma

Leukemias and lymphomas may be analyzed from any solid tissue, blood, bone marrow or other fluids (e.g. cerebrospinal fluid, bronchoalveolar lavage, pleural and peritoneal fluids). Flow cytometry may be performed on peripheral blood and fine needle aspirate material, thus avoiding more invasive procedures for diagnosis. The presence or absence of antigens is determined using an appropriate antibody panel for differential diagnosis. This process may be necessary at the initial diagnostic phase, for evaluation of separate hematologic malignancies, or when tumor is present in several anatomic sites. It may also be necessary where there is abnormal tissue, bone marrow or blood histology, where results are suspicious for lymphoma or leukemia, and where the physician must distinguish reactive from neoplastic conditions; and morphologic exam is not sufficiently sensitive to resolve the diagnosis (e.g. minimal disease, either denovo or residual, after therapy).

Once a specimen is received the pathologist assesses the clinical history, reviews the morphology of the specimen (ie. blood smear, bone marrow smear, and lymph node) and determines if the lesion is amenable to analysis by flow cytometry. This is a key step, as the initial clinical and or morphologic examination of the specimen may distinguish among potential “mature” lymphoproliferative disorders, acute leukemias and other conditions that may or may not be appropriate for cytometric evaluation.

Where flow cytometry has previously established a diagnosis, and where the neoplastic cells have a characteristic phenotype, it may be unnecessary to extensively re-phenotype the lesion; instead, a limited analysis may be used that allows the pathologist to definitively identify the abnormal cell population while referring back to the original phenotype. However, this approach may not be appropriate for complex fluid samples (e.g. marrow) or for acute leukemia, where changes in antigen profiles at relapse or post chemotherapy are not uncommon.

Leukemia:

Flow cytometric analysis of blood and marrow mononuclear cells can generally differentiate between polyclonal and monoclonal (monotypic) B cell lymphoproliferative disorders or lymphoid neoplasms. It can also define certain atypical gains and losses of T cell related antigens that are associated with clonal T cell lymphoproliferations.

At a minimum, flow cytometric analysis for mature B cell or T-cell lymphoproliferations should evaluate leukemic cells for expression of multiple pan B-cell or T-cell lymphoid differentiation antigens, intrinsic (non-Fc bound) surface immunoglobulins, light chains (kappa and lambda), and additional leukocyte antigens, that help to distinguish between the various T or B cell leukemias. Additional antigens, such as CD38 and ZAP70, may provide prognostic information.

In the situation of plasma cell neoplasms (e.g. myeloma, MGUS), a smaller panel directed at both cell surface and cytoplasmic immunoglobulin light chains would be appropriate. The acute leukemic panel is designed to distinguish whether leukemic blasts are of myeloid or lymphoid origin and if the latter, whether they are T or B lineage. For the B cell lineage certain differentiation antigens are prognostically useful.

The acute leukemia panel may also be necessary for the detection of minimal residual disease in post-therapy bone marrow samples from leukemic patients. Because of the need to define the presence of a given atypical profile, both the initial and post therapy panels require additional antigens to fully characterize the neoplastic cells.

Myelodysplasia (MDS)

Flow cytometric immunophenotyping is also useful in immunophenotyping MDS, because it allows for the detection of an accurate percentage of myeloblasts; microblasts are characteristic of MDS and often difficult to morphologically differentiate from lymphocytes. Also of interest, the use of 4-color flow cytometry has allowed for the identification of abnormal myeloid populations in more than 90% of non-chronic myeloid leukemia myeloproliferative disorders (MPDs) and MDSs with a clonal cytogenetic abnormality, supporting the use of FCI in the diagnosis of these disorders. Flow cytometric immunophenotyping may also allow for the detection of an accurate percentage of monocytic cells, by analyzing CD14 and CD64, in establishing a diagnosis of chronic myelomonocytic leukemia (CMML). In addition, the morphologically mature monocytes of CMML may reveal abnormalities by FCI (partial loss of CD13, CD14, and CD15 and expression of CD56) that are not observed in normal monocytes. These abnormalities may indicate clues to a correct classification of CMML in these cases. (Dunphy)

Lymphoma

An adequate biopsy is key to diagnosis and staging of lymphomas, and is often diagnostic in and of itself. Flow cytometry is usually a secondary test. However some lymphoid proliferations can be morphologically confused with lymphoma. Further the use of fine needle aspirate biopsy (FNA) results in the loss of the biopsy architecture, a key feature in distinguishing benign from neoplastic lymphoproliferations. Lastly, the biopsy and FNA are not always able to distinguish clinically significant forms of lymphoma (e.g. mantle cell NHL). All of these situations are indications for flow cytometry and assist with the diagnosis, the prognosis, and the treatment of patients with lymphoma.

The panel of antibodies to leukocyte antigens are designed to identify and characterize lymphoproliferative disorders, which are usually comprised of mature B, T or plasma cells. Flow cytometric testing on blood or bone marrow for anaplastic large cell lymphoma, lymphomatoid granulomatosis (LYG), thymic B cell lymphoma, diffuse large B-cell lymphoma, plasma cell neoplasms or large cell lymphoma must be cautiously interpreted because of false negative results due to tumor cell loss in this disease population.

For B cell malignancies, demonstration of the presence of monoclonal population by restricted kappa or lambda, immunoglobulin light chain expression is useful, particularly when augmented by other differentiation antigens. These combined with a pan B antigen can not only help support the diagnosis of neoplasia, but significantly assist in defining the specific type of B cell lymphoma.

For T cell proliferations, clonality can usually be assessed using two complementary approaches. The first and newest is to use well-defined panels of 20 antibodies to TCR V beta genes. The other, more indirect method looks for atypical absence of well-defined pan T antigens and /or atypical intensities of pan T antigens may serve as reasonably specific markers of clonality.

Lastly, atypical coexpression of certain antigens is helpful in defining certain subsets of T cell lymphomas. To render a formal diagnosis of T cell lymphoma, such flow data needs to be correlated with morphology and in some instances TCR gene clonality, HTLV serologic and or cytogenetic studies.

In the situation of plasma cell neoplasm (e.g. plasma cytoma) a smaller panel directed at both cell surface immunoglobulin light chains and cytoplasmic immunoglobulin light chains would be appropriate.

Flow cytometry can help define Natural Killer (NK) cell lineage in rare neoplastic NK proliferations

Expression of the KIR family of NK-cell receptors has been used as a surrogate marker for clonality in NK cell disorders. For example, in chronic lymphoproliferative disorders of NK cells, expression of the KIR family is abnormal—either restricted isoform expression or a complete lack of detectable expression. Evaluation of KIR expression by flow cytometry can thus be used as evidence of a chronic NK-cell lymphoproliferative disorder versus a reactive NK-cell proliferation?

However, there are no immunophenotypic markers for clonality. In these instances, careful correlation with clinical course or molecular or cytogenetic testing may assist.

The panel would be performed in stages and may include up to 20 antibodies for lymphomas.

2. Histiocytic and Mast Cells

In the premier diagnostic text for hematopathology, World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues, the demonstration of an aberrant mast cell phenotype is listed as independent criteria for the diagnosis of mast cell disease. This diagnostic criteria is based upon immunohistochemistry or flow cytometry. However, within the literature, the advantage of flow cytometric analysis in the detection and evaluation of mast cells has been touted due to the high sensitivity and objectivity that multiparametric analysis of a high number of cells can afford. Flow cytometry in mast cell evaluation is also of utility because it can aid in the identification of coexisting hematological malignancies, such as lymphoma, acute myeloid leukemia, myelodysplasia, and chronic myeloproliferative disorders that can accompany systemic mastocytosis in roughly one third of cases.

3. Lymphocytosis (symptomatic)

Flow cytometry may be indicated when signs and symptoms may suggest the presence of hematolymphoid neoplasm, and where flow cytometry is a useful tool in establishing the primary diagnosis. Flow cytometry is indicated where the up front utilization have a reasonable likelihood of diagnostic yield. These diagnoses include absolute lymphocytosis, lymphadenopathy and splenomegaly. This does not mean that it is necessary to randomly check lymphoproliferative disorders in peripheral blood specimens.

4. Enlargement of lymph nodes

Because of its increased specificity and in some cases increased sensitivity, flow cytometry has emerged as a primary diagnostic modality in the diagnosis of non-Hodgkin lymphoma and lymphoproliferative neoplasms and is no longer considered an ancillary tool. There is significant consensus to show the effectiveness of flow cytometry in diagnosing hematolymphoid neoplasms in the absence of obvious morphologic abnormalities. Delaying the ordering of flow cytometry until there is a review of the histologic sections because flow cytometry requires fresh tissue and even within 24 hours, the viability of neoplastic cells is reduced.

5. Transplants:

Organ Transplants:

Postoperative monitoring of organ transplants may be necessary to determine early rejection, immunosuppressive therapy toxicity, or differentiation of infection from allograft rejection. The cell surface marker examined is CD3. This may require repeated analysis when symptoms are expressed for the above conditions by the transplant patient. Flow cytometry is also used in the evaluation for the presence of a post transplant lymphoproliferative disorder.

Stem cell transplants:

To measure stem cell counts (e.g. CD34, CD45) in patients undergoing autologous transplantation.

6. Primary Immunodeficiencies

Primary immunodeficiencies (e.g., Lymphocyte disorders, Phagocyte disorders, Monocyte/macrophage disorders, Chronic Granulomatous Disease) are immune disorders that are present at birth. These conditions are quite rare. Diagnosis typically occurs at an early age due to recurrent infections with frequent treatment failures. Initial evaluation for suspected primary immunodeficiencies includes physical exam, laboratory evaluation (e.g., CBC, platelet, WBC with differential, ESR), and may include skin testing. Flow cytometry is indicated for diagnostic purposes in the presence of established disease or when abnormal results are found in the initial evaluation.

7. Paroxysmal Nocturnal Hemoglobinuria

Paroxysmal nocturnal hemoglobinuria is a disease in which blood cells are unusually sensitive to lysis by complement. This condition is caused by a genetic mutation that results in the absence of over a dozen surface antigens on red and white blood cells. It can be diagnosed very efficiently by assessing both the red and white blood cells by flow cytometry for the absence of these antigens. In general staining both the red and white blood cells with fluorescent inactivated aureolysin (FLAER) and/or with antibodies to some of the missing GPI anchored antigens (such as CD59, CD14 and CD55) will allow for a very rapid and accurate diagnosis.

8. HIV infection

The clinical status of an HIV-infected patient can be monitored by the analysis of the surface antigens CD4 and CD8. This information can contribute to a staging as well as medical management for that individual (e.g., the need for drug therapy or prophylaxis). Monitoring would be considered appropriate no greater in frequency than once every 3 months. When a patient is stable, especially during the long period of clinical latency, assays would be appropriate at a frequency less often. When the patient has an acute problem and/or therapy change, it may be necessary to perform the test at an increased frequency.

Note: In addition to flow cytometry other tests are used to evaluate and follow this disease such as: T cell; total count and or T cell absolute CD4 and CD8 count including ratio.

On initial evaluation, additional T cell markers may be indicated.

When flow is being used for lymphocyte subset quantification the following codes within the immunology section of CPT should be considered:

86355 B cells, total count

86356 Mononuclear cell antigen, quantitative (e.g., flow cytometry), not otherwise specified, each antigen

86357 Natural killer (NK) cells, total count

86359 T cells; total count

86360 T cells; absolute CD4 and CD 8 count, including ratio

86361 T cells; absolute CD4 count

86367 Stem cells (i.e., CD34) total count

(These codes are informational only to this document.)

9. Drug monitoring

Drugs that react against specific monoclonal antibodies are being developed to treat certain diseases that impact the immune system. (Examples of 2 drugs that would fit into this category are Alefacept and Alemtuzumab).

10. Hereditary Persistence of Fetal Hemoglobin (HPFH)

Hereditary persistence of fetal hemoglobin (HPFH) is a group of disorders in which hemoglobin F (the dominant hemoglobin in the developing fetus) persists into adult life. By itself this disorder is usually clinically benign. However, HPFH is sometimes inherited together with thalassemias and other hemoglobinopathies such as hemoglobin S (sickle cell trait). In these latter conditions, the presence of high levels of hemoglobin F modify the clinical severity of the thalassemia or the hemoglobin S disorder. Complicating matters though is the observation that some patients with sickle cell disease have an increase in hemoglobin F levels that is not due to HPFH. These patients can have a relatively severe clinical course. Thus it is critical to separate patients with homozygous hemoglobin S and physiologic increases in hemoglobin F levels from patients with heterozygous hemoglobin S and HPFH. Flow cytometry is a very effective way to distinguish between these two conditions. In most cases of HPFH every red blood cell has about the same amount of hemoglobin F (called a "homocellular distribution") whereas in physiologic increases in hemoglobin F, the concentration of hemoglobin F varies from one red blood cell to the next (called a "heterocellular distribution"). Using antibodies to hemoglobin F, flow cytometry can readily distinguish a homocellular from a heterocellular hemoglobin F distribution and therefore distinguish HPFH from physiologic increases in hemoglobin F. The test would be indicated in anyone with an unexplained increase in hemoglobin F.

11. Hereditary Spherocytosis

A recently developed fluorescent dye method has great utility in the diagnosis of hereditary spherocytosis. In the past the diagnosis of hereditary spherocytosis was based on recognizing spherocytes on the peripheral blood smears and by performing a test called the osmotic fragility test. The osmotic fragility test is sensitive and picks up most patients with hereditary spherocytosis, but it lacks specificity, because patients with other causes of hemolytic anemia can have an abnormal osmotic fragility result. Using flow cytometry with a fluorescent dye (eosin-5-maleimide) one can distinguish hereditary spherocytosis (the red blood cells have weaker staining with the dye) from other causes of spherocytosis (the red blood cells have normal binding to the dye). When coupled with the traditional tests (osmotic fragility and review of blood cell morphology), this has proven to be a very useful test. Flow cytometry for hereditary spherocytosis would be indicated in patients who have Coombs' negative hemolytic anemia.

12. HLA B27

An increased incidence of the HLA-B27 antigen has been reported in patients with ankylosing spondylitis, Reiter's syndrome, anterior uveitis, psoriatic arthritis, and inflammatory bowel disease. As a result, tests for the HLA-B27 antigen are a valuable adjunct in the diagnosis of these diseases. Traditionally, it has been the lymphocytotoxicity assay (86812) that was used to determine HLA status. The development of monoclonal antibodies to HLA antigens has rendered flow cytometry an alternative procedure.

13. Flow cytometry Analysis of Platelets

The use of flow cytometry in the quantitative and qualitative analysis of platelets is becoming more evident and will likely be part of the work-up of coagulation defects of primary and secondary hemostasis in the near future. For example, flow cytometry has been utilized for analysis of platelets in quantitative and qualitative disorders such as Glanzmann Thrombasthenia (GT) and Bernard-Soulier Disease.

GT is a rare inherited or acquired platelet disorder that derives from a defective GPIIa/GPIIb receptor.

Normally, the GPIIa/GPIIb receptor is involved in platelet cross linking by serving as a receptor for fibrin, thereby creating the initial platelet plug at the site of endothelial injury. Absence of this receptor results in increased susceptibility to bleeding. As demonstrated by Jennings, platelets with decreased expression or absence of the GPIIa/GPIIb receptor can be easily distinguished in patients with GT by flow cytometry.

Demonstration of decreased surface expression provides evidence as to the presence of hereditary GT.

Acquired GT is more of an autoimmune phenomenon with the presence of GPIIb/GPIIIa blocking antibodies.

Giannini et al, recently reported the ability to use flow as a rapid test to determine both the functional effect and identity of the molecular targets of these antibodies.

Bernard-Soulier (B-S) Disease is another rare inherited disorder that prevents the initial binding of platelets at the site of endothelial injury by absence of or presence of abnormal surface GPIa/V/IX receptor. Abnormalities of this receptor thereby prevent attachment of platelets to subendothelial or free von Willebrand's factor with subsequent tendency to bleed. Flow cytometry can be used to measure antibodies directed at specific loci of the GPIa/V/IX receptor which include GPIb (CD42b), GPIX (CD42a), and GPV (CD42d). Another characteristic of B-S Disease that can be utilized in the initial evaluation of the flow cytometric data is the size of platelets. In B-S disease platelets are generally larger than normal and may demonstrate an increase spectrum of size that can be distinguished from fragmented RBCs and debris by specific binding of antibodies directed to the GPIb/IX/V receptor, as previously mentioned.

B. DNA content (ploidy) and cell proliferative activity (S-phase fraction or %S-phase) (88182) Flow cytometry; cell cycle or DNA analysis.

1. Molar Pregnancies

Flow cytometry has also been proven to be useful in evaluating molar and partial molar pregnancies. Using a method to quantify DNA, similar to that used for evaluation of carcinomas, partial moles, which are triploid, can be readily distinguished from normal placenta and complete molar pregnancies (which are usually diploid). This is a very important clinical distinction and is a valid indication for flow cytometry.

2. Carcinomas

DNA analysis of tumor for ploidy and percent-S-phase cells may be necessary for selective patients with carcinomas. Information obtained from flow cytometry is useful when the obtained prognostic information will affect treatment decisions in patients with low stage (localized disease). These tests are not indicated for prognostic and therapeutic purposes in the routine clinical management of cancers. Some of the reasons for this are: Ploidy status may have uncertain value in individual patients depending on a number of factors that can include specimen size, source, and preparation; and that aneuploidy has been detected in non-tumor cells.

Increased S-phase activity is a more accepted prognostic indicator but it is technically more difficult to measure accurately. Not all tumors with S-phase fraction are malignant; not all tumors with increased S-phase metastasize; and not all malignant tumors with relatively small S-phase fraction fail to metastasize.

It has not been proven that this testing provides useful information in colorectal or breast cancers.

This is usually performed only one time after a diagnosis has been made and before treatment is initiated.

This testing is indicated for selected patients (without metastatic disease) with the following conditions:

- a. Prostatic adenocarcinoma
- b. Urinary Bladder Carcinoma
- c. Ovarian Carcinoma
- d. Endometrial adenocarcinoma

- e. Renal cell adenocarcinoma
- f. Mediastinal neuroblastoma
- g. Medulloblastoma

Coding Information

Bill Type Codes:

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

12x	Hospital-inpatient or home health visits (Part B only)
13x	Hospital-outpatient (HHA-A also) (under OPPTS 13X must be used for ASC claims submitted for OPPTS payment -- eff. 7/00)
14x	Non-Patient Laboratory Specimens
18x	Hospital-swing beds
21x	SNF-inpatient, Part A
22x	SNF-inpatient or home health visits (Part B only)
23x	SNF-outpatient (HHA-A also)
71x	Clinic-rural health
73x	Clinic-independent provider based FQHC (eff 10/91)
85x	Special facility or ASC surgery-rural primary care hospital (eff 10/94)

Revenue Codes:

Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory; unless specified in the policy services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

Revenue Codes

Contractors may specify Revenue Codes to help provider's identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory; unless specified in the policy services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

030X

Laboratory-general classification

CPT/HCPCS Codes

88182	FLOW CYTOMETRY, CELL CYCLE OR DNA ANALYSIS
88184	FLOW CYTOMETRY, CELL SURFACE, CYTOPLASMIC, OR NUCLEAR MARKER, TECHNICAL COMPONENT ONLY; FIRST MARKER
88185	FLOW CYTOMETRY, CELL SURFACE, CYTOPLASMIC, OR NUCLEAR MARKER, TECHNICAL COMPONENT ONLY; EACH ADDITIONAL MARKER (LIST SEPARATELY IN ADDITION TO CODE FOR FIRST MARKER)
88187	FLOW CYTOMETRY, INTERPRETATION; 2 TO 8 MARKERS
88188	FLOW CYTOMETRY, INTERPRETATION; 9 TO 15 MARKERS
88189	FLOW CYTOMETRY, INTERPRETATION; 16 OR MORE MARKERS

ICD-9 Codes that Support Medical Necessity

ICD-9 Codes that Support Medical Necessity

Note: ICD-9 codes must be coded to the highest level of specificity.

A. CPT codes 88184-88189 are indicated for the following conditions:

1. HIV infection (ICD-9 042, 079.51, 079.52, 079.53, V0.8), as defined by the Center for Disease Control criteria.
2. Leukemias (ICD-9 204.00-208.92)
3. Lymphomas (ICD-9 200.00-203.82)
4. Abnormal tissue, bone marrow, or blood histology when the results are suspicious for lymphoma, leukemia or MDS and where the physician must distinguish reactive from neoplastic conditions (ICD-9 238.6, 238.71-238.79, 285.9, 287.30-287.5, 795.4).
5. Platelet defects (ICD-9 287.1)
6. Postoperative monitoring of organ transplant patients (ICD-9 996.80-996.89, V42.0-V42.89).
7. Pretransplant evaluation of allogenic or autologous donor cells (V42.82)
8. Primary immunodeficiencies (ICD-9 279.10-279.9, 288.09, 334.8)
9. Monoclonal gammopathies (ICD-9 273.1, 273.3)
10. Certain anemias:
 - Acquired hemolytic anemia, unspecified 283.9
 - Constitutional aplastic anemia 284.0
 - Constitutional red cell aplasia 284.01
 - Other constitutional aplastic anemia 284.09
 - Pancytopenia -myelophthisis 284.1 - 284.2
 - Other specified aplastic anemia 284.89
 - Aplastic anemia, unspecified 284.9
 - Sideroblastic anemia 285.0
 - Anemia in neoplastic disease 285.22
 - Other anemia 285.8 - 285.9
11. Diseases of white blood cells
 - Neutropenia, unspecified - neutropenia due to Infection 288.00 - 288.04

Other neutropenia 288.09
 Functional disorders of polymorphonuclear Neutrophils - hemophagocytic syndromes 288.1 - 288.4
 Leukocytopenia, unspecified – lymphocytopenia 288.50 - 288.51
 Other decreased white blood cell count 288.59
 Leukocytosis, unspecified - basophilia 288.60 - 288.65
 Other elevated white blood cell count 288.69
 Other specified diseases of white blood cells 288.8 - 288.9
 12. Certain hemolytic anemias:
 Paroxysmal nocturnal hemoglobinuria (ICD-9 283.2)
 Portal vein thrombosis 452
 Embolism of vein thrombosis, unspecified 453.9
 Hereditary spherocytosis (ICD-9 282.0)
 Sickle cell (ICD-9 282.5, 282.60-282.69)
 HPFH (ICD-9 282.7)
 13. Drug monitoring (ICD-9 V58.69)
 14. Conditions associated with gene HLA B27
 Reiter's syndrome (ICD-9 099.3)
 Uveitis (ICD-9 364.3)
 Psoriatic arthritis (ICD-9 696.0)
 Juvenile arthritis (ICD-9 714.30)
 Ankylosing spondylitis (ICD-9 720.0-720.9)
 Inflammatory bowel disease (ICD-9 555.0-556.9)
 15. Splenomegaly (ICD-9 789.2)
 16. Abdominal mass (ICD-9 789.30- 789.39)

B. CPT code 88182 (Flow cytometry; cell cycle or DNA analysis) is indicated for selected patients (without metastatic disease) with the following conditions:

1. Prostatic adenocarcinoma (ICD-9 185)
2. Urinary Bladder Carcinoma (ICD-9 188.0-188.9)
3. Ovarian Carcinoma (ICD-9 183.0, 183.8)
4. Endometrial adenocarcinoma (ICD-9 182.0)
5. Renal cell adenocarcinoma (ICD-9 189.0, 189.1)
6. Mediastinal neuroblastoma (ICD-9 164.2, 164.3)
7. Medulloblastoma (ICD-9 191.0-191.8)
8. Molar pregnancy (ICD-9 630)

XX000

Not Applicable

Diagnoses that Support Medical Necessity

ICD-9 Codes that DO NOT Support Medical Necessity

ICD-9 Codes that DO NOT Support Medical Necessity Asterisk Explanation

Diagnoses that DO NOT Support Medical Necessity

General Information

Documentation Requirements

Documentation Requirements

Documentation supporting the medical necessity of this item, such as ICD-9 codes, must be submitted with each claim. Claims submitted without such evidence will be denied as being not medically necessary.

Documentation in the progress notes and/or in the pathology report(s) must reflect medical necessity, and be available on request.

Appendices

Utilization Guidelines

Utilization Guidelines

Routine use of flow cytometry in situations where the test is performed on tissue or tumor tissue is not covered. Documentation in the patient's record must demonstrate how the results would impact the treatment plan.

Acute leukemia: Up to 20 antibodies may be required to adequately characterize acute leukemia.

Chronic lymphoproliferative disorder (CLD): Up to 20 antibodies may be required to adequately characterize CLD.

Lymphoma: Up to 20 antibodies may be required to adequately characterize lymphoma.

Plasma cell dyscrasia: Up to 8 antibodies may be required to adequately characterize plasma cell dyscrasia.

Rare cases are diagnostic problems and may require more antibodies to characterize the disease process. Such problems should be documented in the flow cytometry narrative report.

Performing duplicate testing on different sources (i.e. blood smear and bone marrow) from the same patient in the same time frame may sometimes be necessary.

Examples:

The lymph node flow is performed in order to render the diagnosis of lymphoma as well as subtype the malignancy, in order to "grade" the tumor. The bone marrow flow is done to "stage" the tumor by identifying malignancy within the bone marrow compartment. Both the grade and stage are separate data that are required prior to initiating appropriate therapy.

Similarly, flow may be performed on a lymph node and a pleural effusion, or a bone marrow and pleural effusion on the same day of service when the possibility of a malignant effusion is also suspected. As a practicing pathologist, I can relate the significant benefits that flow offers traditional cytology in these cases, that a competent pathologist may not otherwise be able to render a definitive diagnosis.

Flow cytometry used as part of experimental protocols is not a covered service.

The CPT codes, descriptors and two digit modifiers used in this policy are copyright by the American Medical Association. All rights reserved.

Comments

A. Terms:

ploidy: The number of single sets of chromosomes in a cell or organism.

diploid: Having two sets or a pair of chromosomes as normally found in the somatic cell of higher organisms.

A diploid cell has one chromosome from each parent.

triploid: Having three times the haploid number of chromosomes in the cell nucleus and would be abnormal in humans.

aneuploid: Having a chromosome number that is not an exact multiple of the normal diploid number, with either fewer or more than the normal number of chromosomes in the cell. In humans, an aneuploid cell would be considered abnormal. A triploid cell would be an example of aneuploidy in humans.

B. Flow cytometry is a dynamic field. We will evaluate any requests for extension of coverage that are supported by peer-reviewed literature.

*- An asterisk indicates a revision to that section of the policy.

This policy does not reflect the sole opinion of the contractor or Contractor Medical Director. Although the final decision rests with the MAC contractor this policy was developed in cooperation with advisory groups which include representatives from various specialties, and adapted for the purpose of converting to MAC jurisdiction.

Sources of Information and Basis for Decision

Sources of Information and Basis for Decision

CLIC-AAAAI, Practice Parameters for the Diagnosis and Management of Immunodeficiency, *Annals of Allergy, Asthma, & Immunology*, August 31, 1995, pp 282-294

Wright, et, al, A Characterization of Common Variable Immunodeficiency: Identification of a Subset of Patients with Distinctive Immunophenotypic and Clinical Features, *Blood*, Vol 76, No. 10 (November 15), 1990, pp 2046-2051

Schmalstieg, et, al, Postnatal Development of T Lymphocytes in a Novel X-Linked Immunodeficiency Disease, *Clinical Immunology and Immunopathology*, Vol 64, No. 1, July 1992, pp 71-77

Jaffe, et, al, Functional Abnormalities of CD8+ T cells defined a Unique Subset of Patients with Common Variable Immunodeficiency, *Blood*, Vol 82, No 1 (July 1) 1993, pp192-201

Mathews, et, al, A Function of the Interleukin-2 (IL-2) Receptor G-Chain in Biologic Responses of X-Linked Severe Combined Immunodeficient B Cells to IL-2, IL-4, IL-13, and IL-15", *Blood*, Vol 85, No1 (January 1), 1995, pp 38-42

Ochs, et, al, Antibody Responses to Bacteriophage fX174 in Patients with Adenosine Deaminase Deficiency@, *Blood*, Vol 80, No 5 (September 1), 1992, pp 1163-1171

Williams Hematology Fifth Edition, McGraw-Hill, Inc., 1995

Pathology Second Edition, J.B. Lippincott Company, 1994

National Cancer Institute Laboratory Protocols

Verstovsek G, et al., Large B-cell lymphomas: Fine needle aspiration plays an important role in initial diagnosis of cases which are falsely negative by flow cytometry; *Diagnostic Cytopathology*; Vol 27, Issue 5, 10/2002, pp282-285

Brodsky, R.A., et al., Improved detection and characterization of paroxysmal nocturnal hemoglobinuria using fluorescent aerolysin, *Am J Clin Pathol*, 2000. 114(3): p. 459-66.

Hoyer, J.D., et al., Flow cytometric measurement of hemoglobin F in RBCs: diagnostic usefulness in the distinction of hereditary persistence of fetal hemoglobin (HPFH) and hemoglobin S-hPFH from other conditions with elevated levels of hemoglobin F. *Am J Clin Pathol*, 2002. 117(6): p. 857-63.

King, M.J., et al., Rapid flow cytometric test for the diagnosis of membrane cytoskeletal associated hemolytic anemia. *Br J Haematol*, 2000. 111: p. 924-933.

Stoya, G., et al., Flow cytometric analysis of band 3 protein of human erythrocytes. *Acta Histochem*, 1997. 99(1): p. 29-36.

Fukunaga, M., Early partial hydatidiform mole: prevalence, histopathology, DNA ploidy, and persistence rate. *Virchows Arch*, 2000. 437(2): p. 180-4.

Fukunaga, M., Flow cytometric and clinicopathologic study of complete hydatidiform moles with special reference to the significance of cytometric aneuploidy. *Gynecol Oncol*, 2001. 81(1): p. 67-70.

Braylan, R.C., et al., U.S.-Canadian Consensus recommendations on the immunophenotypic analysis of hematologic neoplasia by flow cytometry: data reporting. *Cytometry*, 1997. 30(5): p. 245-8.

Braylan, R.C., et al., Optimal number of reagents required to evaluate hematology neoplasias: results of an international consensus meeting. *Cytometry*, 2001. 46(1): p. 23-7.

Hanson, C.A., et al., Immunophenotypic analysis of peripheral blood and bone marrow in the staging of B-cell malignant lymphoma. *Blood*, 1999. 94(11): p. 3889-96.

2000 update on recommendations for the use of tumor markers in breast and colorectal cancer; Clinical Practice Guidelines of the American Society of Clinical Oncology; *J.Clin.Ocol.* 2001; 19(6): 1865-1878

Davis, Bruce H., et al; U.S.- Canadian Consensus Recommendations on Immunophenotypic Analysis of Hematologic Neoplasia by Flow Cytometry: Medical Indications; *Cytometry* 1997 30:249-263

Stewart, Carleton C., et al; U.S. Canadian Consensus Recommendations on the Immunophenotypic Analysis of Hematologic Neoplasia by Flow Cytometry: Selection of Antibody Combinations; *Cytometry* 1997 30: 231-235

Hassett, Joseph; Parker, John; Laboratory Practices in Reporting Flow Cytometry Phenotyping Results for Leukemia/Lymphoma Specimens: Results of Survey; *Cytometry* 1995; 22: 264-281

McCoy, J. Philip; Davis, Bruce; Report of the Clinical Practice Task Force Survey of the Clinical Cytometric Society; *Cytometry* 2001; 46: 177-183

McCoy, J., Philip; Overton, W.R; A survey of Current Practices in Clinical Flow Cytometry, *AJCP* 1996; Vol 106 No.1 82-86

Swedlow SH, Campo E., Harris NL et al. editors, World Health Organization Classification of Tumours of Haematopoietic and Lymphoid tissues, 4th ed., Lyon France: IARC Press, 2008, p. 56

Esribano, L, Montero AC, Nunez R, et al, Flow cytometric analysis of normal and neoplastic mast cells; role in diagnosis and follow-up of mast cell disease; *Immunol Allergy Clin N AM* 2006; 26: 535-47

Esribano, L, Diaz-Augustin B, Lopez A, et al. Immunophenotypic analysis of mast cells in mastocytosis: when and how to do it Proposal Spanish network on mastocytosis (REMA); *Cytometry Part B (Clinical Cytometry)*; 2004; 58B: 1-8

Craig FE, Foon KA; Flow cytometric immunophenotyping for hematologic neoplasms; *Blood* 2008: 111:3962

Davis BH, Holden JT, Bene MC, et al., 2006 Bethesda international consensus recommendations on immunophenotypic analysis of hematology neoplasia: medical indications; *Cytometry Part B Clin Cytom.* 2007: 72B:S5-S13

Andrews JM, Criser DL, Myers JB; Using Peripheral smear review, age and absolute lymphocyte count as predictors of abnormal peripheral blood smear lymphocytosis diagnosed by flow cytometry; *Leuk Lymphoma* 2008; 49 (9): 1731-7

Eley T, Alsawah M, Malsz J, Douglas-Nilitin V; Evaluation of Peripheral blood flow cytometry as a screening tool for non-Hodgkin Lymphoma; *Arch Pathol Lab Med* 2008; 132: 1461: A28

Dunphy, Cherie H.; Applications of Flow Cytometry and Immunohistochemistry to Diagnostic Hematopathology; *Arch Pathol Lab Med*, Vol 128, September 2004

Keren DF, Hanson CA, Hurtubise PE. Flow cytometry in clinical diagnosis: 4th edition. Chicago: ASCP Press, 2007: 306-312.

Michelson AD.; Flow cytometric analysis of platelet surface glycoproteins: phenotypically distinct subpopulation of platelet in chigger with chronic myeloid leukemia; *J Lab Clin Med* 1987; 110: 346-354.

Jennings LK, Ashmun RA, Wang WC, Dockter ME.; Analysis of human platelet glycoproteins IIb-IIIa and Glanzmann's thrombasthenia in whole blood by flow cytometry; *Blood* 1986; 68: 173-179.

Linden M, Felinger AL, Barnard MR, Przyklenk K, Furman MI, Michelson AD; Application of Flow Cytometry to Platelet Disorders; *Seminars in Thrombosis and Hemostasis* 2004; 30(5): 501-511.

Jennings LK, Ashmun RA, Wang WC, et al.; Analysis of human platelet glycoproteins IIb-IIIa and Glanzmann's thrombasthenia in whole blood by flow cytometry; *Blood* 1986; 68: 173-179.

Marti GE, Magruder L, Schuette WE, et al.; Flow cytometric analysis of platelet surface antigens. *Cytometry*; 1988; 9: 448-455.

Wall JE, Buijs-Wilts M, Arnold JT, et al.; A flow cytometric assay using mepacrine for study of uptake and release of platelet dense granule contents; *Br J Haematol* 1995; 89:380-385.

Gordon N, Thom J, Cole C, Baker R.; Rapid detection of hereditary and acquired storage pool deficiency by flow cytometry; *Br J Haematol* 1995; 89: 117-123.

Giannini S, Mezzasoma AM., Guglielmini G, Rossi R, Falcinelli E, Gresele P. A New Case of Acquired Glanzmann's Thrombasthenia: Diagnostic Value of Flow Cytometry.

Kienast J, Schmitz G. Flow cytometric analysis of thiazole orange uptake by platelets: a diagnostic aid in the evaluation of thrombocytopenic disorders. Blood 1990; 75: 116-121.

Parker, Charles, et al and the International PNH Interest Group; Diagnosis and management of paroxysmal nocturnal hemoglobinuria; Blood, 2005 106: 3699-3709

Other Carrier policies

Advisory Committee Meeting Notes

Meeting Date:

Wisconsin 05/15/2009

Illinois 05/13/2009

Michigan 05/06/2009

Minnesota 05/21/2009

J5 MAC 06/04/2009

Start Date of Comment Period

06/04/2009

End Date of Comment Period

07/20/2009

Start Date of Notice Period

03/01/2010

Revision History Number

X

Revision History Explanation

04/03/2009 Approved

04/03/2009 Entered as draft

05/15/2009 Added other contract numbers

06/30/2009 The contractor number 05392 will no longer be valid as of 8/1/2009 as it will be joining with the W MO number.

12/01/2009, corrected typo for codes 789.30- 789.39

11/19/2009 Released to final

02/01/2010 added ICD-9 codes based on a reconsideration request

Reason for Change

Last Reviewed On Date

01/14/2010

Related Documents

This LCD has no Related Documents.

LCD Attachments

There are no attachments for this LCD.

All Versions

Updated on 01/20/2010 with effective dates 11/16/2009 - N/A

Updated on 11/19/2009 with effective dates 11/16/2009 - N/A