TITLE: BONE MARROW OR STEM CELL (PERIPHERAL OR UMBILICAL CORD BLOOD) TRANSPLANTATION

EFFECTIVE DATE: June 1, 2017

This policy was developed with input from specialists in nephrology, transplants, and oncology, and endorsed by the Medical Policy Committee.

IMPORTANT INFORMATION – PLEASE READ BEFORE USING THIS POLICY

These services may or may not be covered by all Medica plans. Please refer to the member’s plan document for specific coverage information. If there is a difference between this general information and the member’s plan document, the member’s plan document will be used to determine coverage. With respect to Medicare and Minnesota Health Care Programs, this policy will apply unless those programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica utilization management policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica utilization management policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

PURPOSE

To promote consistency between reviewers in utilization management decision-making by providing the criteria that generally determine the medical necessity of bone marrow or stem cell transplantation. The Coverage Issues box below outlines the process for addressing the needs of individuals who do not meet these criteria.

BACKGROUND

I. Definitions

A. **Allogeneic** graft is one in which the donor and recipient are of different genetic origins.

B. **Autologous** bone marrow transplant (ABMT) refers to the removal and storage of some of the patient’s own stem cells for restoring bone marrow function after high dose chemotherapy or radiotherapy.

C. **Bone marrow transplant** (BMT) is the reconstitution of the full hematopoietic system by transfer of the pluripotent cells present in the bone marrow (stem cells). A BMT involves a transplant not only of the donor myeloid, erythroid, and megakaryocytic systems, but also of lymphoid and macrophage-monocyte systems. There are four types of disease for which BMT has been widely utilized:

1. **Genetic disease**
   - For immunologic deficiency diseases, the objective is to replace the recipient’s genetically defective lymphoid system with the normal lymphoid tissue of the donor. For genetic diseases such as thalassemia major, the abnormal marrow must be destroyed and replaced by normal stem cells.

2. **Aplastic anemia**
   - Aplastic anemia, which may result from several causes, is a condition that occurs when the body stops producing enough new blood cells and results in loss of the marrow. A stem cell transplant to rebuild the bone marrow with stem cells from a donor may offer the only successful treatment.

3. **Hematologic malignancy**
   - For leukemia and other hematologic malignancies, the objective is the complete destruction of the malignant cell population and unavoidably, normal stem cells, by intensive chemo-radiotherapy followed by restoration of normal marrow function by the transplanted stem cells.

4. **Non-hematologic malignancy** (Chemotherapy or high-dose chemotherapy with autologous peripheral stem cell/bone marrow rescue [HDC/ABMT]).
   - For patients with poor-prognosis cancer necessitating treatment with high dose therapy, autologous stem cell transplantation rescue may be used in selected conditions to reconstitute the devastated marrow.
### Bone Marrow or Stem Cell (Peripheral or Umbilical Cord Blood) Transplantation

**Medica Policy No.: III-TRA.01**

| **D.** | **Chemosensitive** disease is malignant disease that demonstrates at least a partial response to a course of chemotherapy. |
| **E.** | **Donor Lymphocyte Infusion (DLI),** also known as a donor leukocyte infusion or buffy coat infusion, may be performed following allogeneic transplant. Individuals may be infused with lymphocytes obtained via leukapheresis from the original donor. The DLI attempts to induce a beneficial graft-versus-tumor response or improve the level of engraftment without the need for additional stem cell harvest from the donor. This is not a second stem cell transplant. |
| **F.** | **Stem cell boost** is a Hematopoietic Stem Cell Infusion (HSCI) provided to a transplant recipient to assist with hematopoietic recovery or declining donor chimerism. It is not preceded by a preparative regimen and is not considered a new transplant event. |
| **G.** | **Stem cells** are blood cells at the earliest stage of development in the bone marrow. They can be taken from the bone marrow, peripheral bloodstream, or from umbilical cord blood. |
| **H.** | **Stem Cell Transplant**

1. **Allogeneic stem cell transplant** employs chemotherapy, immunosuppressive agents and/or radiation to provide adequate immunosuppression to permit engraftment of stem cells from a human donor other than the patient him/herself. The intensity of the agents used for immunosuppression may be either myeloablative or non-myeloablative depending on the disease being treated and specific patient characteristics. Stem cells may be obtained from the bone marrow, peripheral blood, or umbilical cord blood. The stem cell donor may be related or unrelated to the potential recipient.

2. **Autologous stem cell transplant** utilizes the patient’s own stem cells to re-establish hematopoietic cell function following intensive doses of chemotherapy, with or without radiation. Stem cells may be obtained from repeated aspirations of bone marrow, peripheral blood or umbilical cord blood.

3. **Non-myeloablative stem cell transplant** (NST)/**Reduced–intensity stem cell transplant** (RIST) is a stem cell transplant in which full ablation does not occur. This transplant provides sufficient immunosuppression to achieve donor engraftment, with less toxicity. It is also called a “mini” transplant.

4. **Tandem Transplant** involves two sequential courses of high dose chemotherapy, each followed by stem cell transplant, within a six-month period.

5. **Umbilical cord blood stem cell transplant** employs the infusion of stem cells obtained from the umbilical cord or placenta of a newborn child. A two antigen (Ag) mismatch is acceptable. Cord blood transplantation in patients weighing more than 40kg often utilizes cord blood from at least two donors (“double cord”).

### I. Substance use disorder, as defined by the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) is a problematic pattern of use of an intoxicating substance leading to clinically significant impairment or distress. The symptoms associated with a substance use disorder fall into four major groupings: impaired control, social impairment, risky use, and pharmacological criteria (i.e., tolerance and withdrawal).

| **J.** | **Syngeneic** graft describes a graft in which the donor and recipient are genetically identical. |
| **K.** | **Transplant or graft** is a portion of the body or a complete organ removed from its natural site and transferred to a separate site in the same or different individual. |
| **L.** | **Transplant evaluation** is a physical and psychosocial exam to determine if an individual is an acceptable candidate for transplantation. The specific exams and tests depend on the individual’s diagnosis and health history and vary from hospital to hospital. Tests may include the following: cardiac evaluation; lung function tests; lab tests, including blood typing, chemistry panels, and serology testing for hepatitis, HIV and other common viruses; appropriate cancer surveillance, as indicated (e.g., colonoscopy, pap smear, mammogram, prostate cancer screening); dental evaluation with treatment of existing problems; and psychosocial evaluation. Additional testing or clearance may be required to address other significant coexisting medical conditions. |
| **M.** | **Treatment response** in medicine, is an improvement related to treatment. A number of disease specific systems exist for measuring response.

1. **A complete response**, in general, is the disappearance of all signs of cancer in response to treatment. This does not always mean the cancer has been cured. Also called complete remission.

2. **A partial response**, in general, is defined as a decrease in the size of a tumor, or in the extent of cancer in the body, in response to treatment. Also called partial remission. |

### II. Comments

A. Refer to Appendices for additional terms, definitions and classification tables.

B. Stem cell source and preparative regimens are at the discretion of the treating physician.

C. Donor lymphocyte infusion following allogeneic stem cell transplant is appropriate for incomplete chimerism.
and disease relapse in the setting of incomplete chimerism. This is not a second stem cell transplant.

D. Chimeric Antigen Receptor Therapy and/or the use of T-cells/natural killer cell protocols provide treatment of the underlying disease and are not considered to be a transplant procedure.

**MEDICAL NECESSITY CRITERIA**

I. Indications for Bone Marrow or Stem Cell Transplant Evaluation

Documentation from the medical record indicates that one of the following criteria are met:

A. For *allogeneic* transplant, documentation from the medical record indicates that the individual has one of the following diagnoses:

1. Leukemia
   a. Acute Lymphocytic Leukemia (ALL)
   b. Acute Myeloid Leukemia (AML)
   c. Chronic Lymphocytic Leukemia (CLL)
   d. Chronic Myeloid Leukemia (CML)
   e. Prolymphocytic Leukemia

2. Lymphoma (*See Appendix 1*)
   a. Hodgkin’s Lymphoma
   b. Small B-Cell Lymphocytic Lymphoma
   c. Follicle Center Lymphoma
   d. Lymphoplasmacytoid Lymphoma/Immunocytoma
   e. Marginal Zone Lymphoma
   f. Burkitt Lymphoma
   g. Diffuse Large Cell Lymphoma
   h. Mantle Cell Lymphoma
   i. Precursor B-Cell Leukemia/Lymphoma
   j. T-Cell Lymphoma

3. Myelodysplastic and Pre-Leukemic Syndromes
   a. Myelodysplastic syndrome (MDS)
   b. Myelofibrosis and related conditions
   c. Chronic Myelomonocytic Leukemia (CMML), including Juvenile Myelomonocytic Leukemia (JMML)

4. Multiple Myeloma/Plasma Cell Disorders
   a. Waldenstrom’s Macroglobulinemia

5. Hematological Disorders
   a. Aplastic Anemia
   b. Blackfan-Diamond Syndrome
   c. Chronic Granulomatous Disease
   d. Congenital Agranulocytosis (Kostmann Syndrome)
   e. Congenital Amegakaryocytic Thrombocytopenia
   f. Dyskeratosis Congenita
   g. Fanconi Anemia (FA)
   h. Paroxysmal Nocturnal Hemoglobinuria (PNH)
   i. Schwachman-Diamond Syndrome (SDS)
   j. Sickle Cell Disease
   k. Thalassemia Major

6. Immunodeficiency Syndromes
   a. CD40 Ligand Deficiency
   b. Chediak-Higashi Syndrome
   c. Gaucher disease type I
   d. Hemophagocytic Lymphohistiocytosis (HLH) (same as familial erythrophagocytic lymphohistiocytosis [FEL])
   e. Immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome
   f. Leukocyte Adhesion Deficiency
   g. Lysosomal storage disease
   h. Niemann-Pick type B
   i. Omenn Syndrome
   j. Severe combined immunodeficiency disease (SCID)
   k. Wiskott-Aldrich Syndrome
   l. X-linked Lymphoproliferative Syndrome
7. Inherited Metabolic Disorders
   a. Adrenoleukodystrophy
   b. Epidermolysis Bullosa
   c. Globoid Cell Leukodystrophy (Krabbe Disease)
   d. Hurler Syndrome (MPS-1)
   e. Hunter Syndrome (MPS II)
   f. Mannosidosis and other liposomal storage diseases
   g. Maroteaux-Lamy Syndrome (MPS-VI)
   h. Metachromatic Leukodystrophy
   i. Mitochondrial Neurogastrointestinal Encephalopathy (MNGIE)
   j. Osteopetrosis (also called marble-bone disease, malignant osteopetrosis, or autosomal recessive osteopetrosis)
   k. Rett Syndrome.

B. For autologous transplant, documentation from the medical record indicates that the individual has one of the following diagnoses:
   1. Leukemia
      a. Acute Lymphoblastic Leukemia (ALL)
      b. Acute Myelogenous Leukemia (AML) (also known as Acute Non-Lymphocytic Leukemia [ANLL])
      c. Prolymphocytic Leukemia
   2. Lymphoma (See Appendix 1)
      a. Hodgkin’s Lymphoma
      b. Non-Hodgkin’s Lymphoma
         i. Follicle center lymphoma
         ii. Lymphoplasmacytoid lymphoma/Immunocytoma
         iii. Marginal zone lymphoma (mucosa-associated lymphoid tissue, splenic, nodal)
         iv. Burkitt lymphoma
         v. Diffuse large cell lymphoma (mediastinal large cell, primary effusion)
         vi. Mantle cell lymphoma
         vii. Precursor B-cell leukemia/lymphoma
         viii. T-cell lymphoma
   3. Multiple Myeloma/Plasma Cell Disorders
      a. Multiple myeloma (Single or Tandem auto is appropriate)
      b. AL Amyloidosis
      c. Waldenstrom’s Macroglobulinemia
      d. POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Gammopathy Skin defects Syndrome)
   4. Germ Cell Tumors (Single or Tandem auto is appropriate for all of the germ cell tumors below)
      a. Testicular Germ Cell Tumor
      b. Ovarian Germ Cell Tumor
      c. Extragonadal Germ Cell Tumor
      d. Seminoma
      e. Choriocarcinoma
      f. Embryonal carcinoma
      g. Mixed germ cell tumors
      h. Teratoma
      i. Yolk sac tumor
   5. Brain Tumors
      a. Medulloblastoma
      b. Primitive PeripheraI Neuro-ectodermal Tumor (PNET)
      c. Oligodendroglialoma
      d. Pineoblastoma
   6. Other Malignancies
      a. Atypical teratoid rhabdoid tumors
      b. Neuroblastoma (Single or Tandem auto is appropriate)
      c. Retinoblastoma
      d. Ewing Sarcoma
      e. Supratentorial ependymoma
      f. Wilms Tumor.
II. Indications For Bone Marrow Or Stem Cell Transplantation

Autologous/allogeneic bone marrow or stem cell transplantation is considered medically necessary when documentation in the medical record indicates that all of the following criteria are met:

A. Individual meets the institution’s eligibility criteria for transplant

B. Individual meets the criteria in Section I

C. The individual meets one of the following criteria:
   1. For adults, Karnofsky performance score greater than 70 (See Appendix 2)
   2. For individuals aged 16 and under, a Lansky performance score greater than 50 (See Appendix 3).

D. Individual demonstrates response to treatment with conventional chemotherapy agents, if this treatment is appropriate.

E. Individual or guardian is able to give informed consent. Individual/guardian and family/social support system are able to comply with the treatment regimen and the necessary follow-up. Inadequate funding to pay for immunosuppressive medications post-transplant is addressed and resolved.

F. For individuals with a recent (24 months) history of substance use disorder, successful completion of a chemical dependency program and 6 months of documented ongoing abstinence.

G. No contraindications present, as demonstrated by all of the following:
   1. No uncorrectable medical condition that would itself markedly shorten life expectancy.
   2. No active systemic or localized infection
   3. No irreversible multi-system organ failure
   4. No HIV infection with detectable viral load and CD4 counts less than 200, acquired immunodeficiency syndrome (AIDS) or history of an AIDS-defining condition that is progressive or recurrent (See Appendix 4)
   5. No active substance use disorder
   6. No irreversible severe brain damage
   7. No limited irreversible rehabilitative potential
   8. No ongoing pattern of noncompliance, psychiatric illness, psychological condition, or limited cognitive ability that would make compliance with a disciplined medical regimen impossible
   9. No lack of psychosocial support as indicated by either no identified caregiver or an uncommitted caregiver.
   10. No inability to obtain informed consent from patient or guardian.

III. Indications For Bone Marrow/Stem Cell Retransplantation

Documentation in the medical records indicates that all of the following criteria are met:

A. The individual has one of the following:
   1. Relapse of original disease
   2. Failure to engraft

B. All of the criteria in section II are met

C. No history of behaviors since the previous transplant that would jeopardize a subsequent transplant.

COVERAGE ISSUES

1. Prior authorization is required for:
   • Bone Marrow and Stem Cell Transplant Evaluation
   • Bone Marrow and Stem Cell Transplantation.

2. Coverage may vary according to the terms of the member’s plan document.

3. For Medicare members, refer to the following criteria, as applicable:

4. Medica has entered into separate contracts with designated facilities to provide transplant-related health services, as described in the member’s plan document.

5. Complex cases require medical director or external review, and as necessary, discussion with the patient’s physician.

6. Underlying co-morbidity that significantly alters the risk/benefit of transplant may preclude transplant eligibility.

7. Coverage of costs related to chemotherapy, drugs, other related supplies and services is limited to individuals who have one of the indications listed and are transplant candidates.

8. Coverage of costs related to collection and storage of umbilical cord blood stem cells is addressed in the...
9. Medical director or external review is required for any of the following procedures if not performed in a clinical trial:
   • Autologous tandem stem cell transplants except for the indications noted in the Medical Necessity Criteria above.
   • Allogeneic tandem stem cell transplants.
10. Use of progenitor/stem cells from bone marrow, peripheral blood or umbilical cord blood for non-conventional indications (such as direct injection into the heart muscle, bone or other body tissue) requires medical director or external review. Please refer to the following related Coverage Policies: Autologous/Allogeneic Stem Cell Infusion for Orthopedic Applications; Stem Cell Therapy for Peripheral Artery Disease; and Cell Therapy for the Treatment of Cardiac Disease.
11. If the Medical Necessity and Coverage Criteria are met, Medica will authorize benefits within the limits in the member’s plan document.
12. If it appears that the Medical Necessity and Coverage Criteria are not met, the individual’s case will be reviewed by the medical director or an external reviewer. Practitioners are advised of the appeal process in their Medica Provider Administrative Manual.

References:
Pre-06/2016 MPC


79. Kouroukis CT, Rumble RB. Stem Cell Transplantation In Multiple Myeloma. Toronto (ON): Cancer Care Ontario (CCO);March 29, 2012.

80. Kouroukis CT, Rumble RB. Stem Cell Transplantation In Primary Systemic Amyloidosis. Toronto (ON): Cancer Care Ontario (CCO);March 29, 2012.

81. Kouroukis CT, Rumble RB, Walker I, Bredeson C, Schuh A. Stem Cell Transplantation In Myelodysplastic Syndromes And Acute Myeloid Leukemia. Toronto (ON): Cancer Care Ontario (CCO);March 29, 2012.


**06/2016 MPC**


**02/2017 MPC**


### APPENDIX 1 – Classification of Lymphoid Malignancies

<table>
<thead>
<tr>
<th><strong>WHO Classification of Lymphoid Malignancies</strong></th>
<th><strong>Hodgkin’s Disease</strong></th>
</tr>
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<tbody>
<tr>
<td><strong>B Cell</strong></td>
<td><strong>T Cell</strong></td>
</tr>
<tr>
<td>Precursor B cell neoplasm</td>
<td>Precursor T cell neoplasm</td>
</tr>
<tr>
<td>Precursor B lymphoblastic leukemia/lymphoma (precursor B cell acute lymphoblastic leukemia)</td>
<td>Precursor T lymphoblastic lymphoma/leukemia (precursor T cell acute lymphoblastic leukemia)</td>
</tr>
<tr>
<td>Mature (peripheral) B cell neoplasms</td>
<td>Mature (peripheral) T cell neoplasms</td>
</tr>
<tr>
<td>B cell chronic lymphocytic leukemia/small lymphocytic lymphoma</td>
<td>T cell prolymphocytic leukemia</td>
</tr>
<tr>
<td>B cell prolymphocytic leukemia</td>
<td>T cell granular lymphocytic leukemia</td>
</tr>
<tr>
<td>Lymphoplasmacytic lymphoma</td>
<td>Aggressive NK cell leukemia</td>
</tr>
<tr>
<td>Splenic marginal zone B cell lymphoma (± villous lymphocytes)</td>
<td>Adult T cell lymphoma/leukemia (HTLV-I+)</td>
</tr>
<tr>
<td>Hairy cell leukemia</td>
<td>Extranodal NK/T cell lymphoma, nasal type</td>
</tr>
<tr>
<td>Plasma cell myeloma/plasmacytoma</td>
<td>Enteropathy-type T cell lymphoma</td>
</tr>
<tr>
<td>Extranodal marginal zone B cell lymphoma of MALT type</td>
<td>Hepatosplenic ß’d T cell lymphoma</td>
</tr>
<tr>
<td>Mantle cell lymphoma</td>
<td>Subcutaneous panniculitis-like T cell lymphoma</td>
</tr>
<tr>
<td>Follicular lymphoma</td>
<td>Mycosis fungoides/Sézary syndrome</td>
</tr>
<tr>
<td>Nodal marginal zone B cell lymphoma (± monocytoid B cells)</td>
<td>Anaplastic large cell lymphoma, primary cutaneous type</td>
</tr>
<tr>
<td>Diffuse large B cell lymphoma</td>
<td>Peripheral T cell lymphoma, not otherwise specified (NOS)</td>
</tr>
<tr>
<td>Burkitt’s lymphoma/Burkitt cell leukemia</td>
<td>Angioimmunoblastic T cell lymphoma</td>
</tr>
<tr>
<td></td>
<td>Anaplastic large cell lymphoma, primary systemic type</td>
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</tbody>
</table>

### APPENDIX 2 – Activities of Daily Living
Karnofsky Performance Scale

<table>
<thead>
<tr>
<th>Able To Carry On Normal Activity</th>
<th>No Special Care Needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>Normal; no complaints; no evidence of disease</td>
</tr>
<tr>
<td>90%</td>
<td>Able to carry on normal activity</td>
</tr>
<tr>
<td>80%</td>
<td>Normal activity with effort</td>
</tr>
<tr>
<td><strong>Unable to Work; Able to Live at Home, Care For Most Personal Needs</strong></td>
<td><strong>A Varying Amount of Assistance is Needed</strong></td>
</tr>
<tr>
<td>70%</td>
<td>Cares for self; unable to carry on normal activity or to do active work</td>
</tr>
<tr>
<td>60%</td>
<td>Requires occasional assistance, but is able to care for most needs</td>
</tr>
<tr>
<td>50%</td>
<td>Requires considerable assistance and frequent medical care</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate to Severe Restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td>40%</td>
</tr>
<tr>
<td>30%</td>
</tr>
<tr>
<td>20%</td>
</tr>
<tr>
<td>10%</td>
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</tbody>
</table>

### APPENDIX 3 – Pediatric Activity
Lansky Performance Scale

<table>
<thead>
<tr>
<th>Able To Carry On Normal Activity</th>
<th>No Special Care Needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>Fully active</td>
</tr>
<tr>
<td>90%</td>
<td>Minor restriction in physically strenuous play</td>
</tr>
<tr>
<td>80%</td>
<td>Restricted in strenuous play, tires more easily, otherwise active</td>
</tr>
<tr>
<td><strong>Mild to Moderate Restriction</strong></td>
<td></td>
</tr>
<tr>
<td>70%</td>
<td>Both greater restriction of, and less time spent in active play</td>
</tr>
<tr>
<td>60%</td>
<td>Ambulatory up to 50 percent of time, limited active play with assistance/supervision</td>
</tr>
<tr>
<td>50%</td>
<td>Considerable assistance required for any active play; fully able to engage in quiet play</td>
</tr>
<tr>
<td><strong>Moderate to Severe Restrictions</strong></td>
<td></td>
</tr>
<tr>
<td>40%</td>
<td>Able to initiate quiet activities</td>
</tr>
<tr>
<td>30%</td>
<td>Needs considerable assistance for quiet activity</td>
</tr>
<tr>
<td>20%</td>
<td>Limited to very passive activity initiated by others (e.g. TV)</td>
</tr>
<tr>
<td>10%</td>
<td>Completely disabled, not even passive play</td>
</tr>
</tbody>
</table>
APPENDIX 4 – AIDS-Defining Conditions

- Bacterial infections, multiple or recurrent*
- Candidiasis of bronchi, trachea, or lungs
- Candidiasis of esophagus
- Cervical cancer, invasive†
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (greater than 1 month’s duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes), onset at age greater than 1 month
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy attributed to HIV§
- Herpes simplex: chronic ulcers (greater than 1 month’s duration) or bronchitis, pneumonitis, or esophagitis (onset at age greater than 1 month)
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (greater than 1 month’s duration)
- Kaposi sarcoma
- Lymphoma, Burkitt (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- Mycobacterium avium complex or Mycobacterium kansasii, disseminated or extrapulmonary
- Mycobacterium tuberculosis of any site, pulmonary†, disseminated, or extrapulmonary
- Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
- Pneumocystis jirovecii (previously known as “Pneumocystis carinii”) pneumonia
- Pneumonia, recurrent†
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia, recurrent
- Toxoplasmosis of brain, onset at age greater than 1 month
- Wasting syndrome attributed to HIV§

* Only among children aged less than 6 years.
† Only among adults, adolescents, and children aged greater than or equal to 6 years.
§ Suggested diagnostic criteria for these illnesses, which might be particularly important for HIV encephalopathy and HIV wasting syndrome, are described in the following references:
  - CDC. 1994 Revised classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR 1994;43(No. RR-12).
  - CDC. 1993 Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. MMWR 1992;41(No. RR-17).