

TITLE: CYTOMEGALOVIRUS IMMUNE GLOBULIN (CMV-IG, CYTOGAM®)
INDICATIONS FOR USE

GUIDELINES:

Cytomegalovirus Immune Globulin (CMV-IG, CytoGam®) is an immunoglobulin G (IgG) containing a standardized amount of antibody to cytomegalovirus (CMV). The purified immunoglobulin is derived from pooled adult human plasma selected for high titers of antibody for CMV. This policy outlines guidelines for the optimal use of CMV-IG. These criteria were developed with adult and pediatric representation from various departments, including Infectious Diseases, Solid Organ Transplantation, Hematology/Oncology/BMT, and Pharmacy.

PURPOSE:

To develop guidelines for the appropriate use of CMV-IG

APPLICABILITY:

All centers

PROCEDURE:

- I. Prior to use, Infectious Diseases Approval is required for all CMV-IG orders (Class III Antimicrobial Agent).
- II. Due to limited data and cost, CMV-IG is only recommended for the following indications:
 - A. CMV Pneumonitis- must meet all of the following criteria:
 1. Bone Marrow Transplant Recipient, Solid Organ Transplant Recipient, HIV/AIDS patient, or other immunosuppressed patient
 2. Evidence of CMV disease (e.g. CMV inclusions) in a lung tissue biopsy
 - a. In cases where biopsy is not possible, CMV viremia along with isolation of CMV from respiratory/BAL sample can replace the need for biopsy proven CMV pneumonitis. In cases in which neither a biopsy nor a respiratory/BAL sample are possible, radiologic findings consistent with CMV pneumonitis along with viremia may replace the need for biopsy proven pneumonitis.
 3. Clinical signs and symptoms of CMV disease of the lung
 4. CMV infection
 - a. CMV infection defined by detection of CMV DNA in blood (positive CMV PCR or pp65 antigenemia) or isolation of CMV

from blood, urine, or organ biopsy by conventional culture or "shell-vial" rapid culture

B. Refractory CMV Disease- must meet all of the following criteria:

1. Bone Marrow Transplant Recipient, Solid Organ Transplant Recipient, HIV/AIDS patient, or other immunosuppressed patient
2. Clinical signs and symptoms of CMV disease of the affected organ
3. CMV infection
 - a. CMV infection defined as detection of CMV DNA in blood (positive CMV PCR or pp65 antigenemia) or isolation of CMV from blood, urine, or organ biopsy by conventional culture or "shell-vial" rapid culture
4. Refractory CMV disease
 - a. Rising (3-fold increase or > 5,000 copies/mL) blood CMV PCR viral load OR worsening clinical symptoms after at least one week of appropriately-dosed treatment with intravenous antiviral(s).
 - i. Alternative and/or combination antiviral therapies should be considered prior to the addition of CMV-IG to a failing antiviral regimen.

C. Prophylaxis in High-Risk Patients Intolerant to Antiviral Prophylaxis

1. Seronegative recipients of seropositive organs may receive prophylaxis with CMV-IG if they do not tolerate a trial of antiviral prophylaxis

III. In cases of refractory disease and/or cases of antiviral resistance, testing for CMV resistance is recommended. The test is performed by a reference laboratory, and gene sequencing identifies two mutations: UL97 (which confers ganciclovir resistance) and UL54 (ganciclovir, foscarnet, and cidofovir resistance). The test does not require growth on culture, is performed Monday to Friday, and turnaround time is approximately 3 days. Four to five milliliters of whole blood should be collected in an EDTA (lavender top) tube and submitted to microbiology. Proven or presumed resistant CMV should be treated with alternative antiviral agent(s) (e.g., foscarnet, cidofovir, ganciclovir+foscarnet, etc.).

IV. **CMV-IG Dosing**

- A. For the treatment of pneumonitis:
 1. **400 mg/kg/dose IV on days 1, 2, and 7 and 200 mg/kg/dose IV on day 14**
- B. Alternative dosing for pneumonitis and/or refractory CMV disease of other organs:
 1. **100 mg/kg/dose IV every other day for 7 doses (14 days)**
- C. Prophylaxis for patients intolerant to antiviral prophylaxis

1. **150 mg/kg/dose IV weekly (or every two weeks) for 4 doses**

- D. Note: each dose should be rounded to nearest 2.5 grams to maximize contents of vials
- E. Note: When utilized in treatment, CMV-IG should always be given in conjunction with systemic antivirals

RESPONSIBILITY:

Joint Subcommittee for Anti-Infective Use

REFERENCES:

Emmanuel D, Cunningham I, Jules-Elysee K, et al. Cytomegalovirus pneumonia after bone marrow transplantation successfully treated with the combination of ganciclovir and high-dose intravenous immune globulin. *Ann Intern Med* 1988; 109: 777-782.

George MJ, Snyderman DR, Werner BG, et al. Use of ganciclovir plus cytomegalovirus immune globulin to treat CMV pneumonia in orthotopic liver transplant recipients. The Boston Center for Liver Transplantation CMVIG-Study Group. *Transplant Proc* 1993; 25(5 Suppl 4): 22-4.

Preiksaitis JK, Brennan DC, Fishman J, et al. Canadian society of transplantation consensus workshop on cytomegalovirus management in solid organ transplantation final report. *Am J Transplant* 2005; 5: 218-227.

Reed EC, Bowden RA, Dandliker PS, et al. Treatment of cytomegalovirus pneumonia with ganciclovir and intravenous cytomegalovirus immunoglobulin in patients with bone marrow transplants. *Ann Intern Med* 1988; 109: 783-788.

Schmidt GM, Kovacs A, Zaia JA, et al. Ganciclovir/immunoglobulin combination therapy for the treatment of human cytomegalovirus-associated interstitial pneumonia in bone marrow allograft recipients. *Transplantation* 1988; 46: 905-907.

Valantine HA, Luikart H, Doyle R, et al. Impact of cytomegalovirus hyperimmune globulin on outcome after cardiothoracic transplantation. *Transplantation* 2001; 72: 1647-1652.

GUIDELINE DATES:

Issued: May 2009

Reviewed: May 2010

Revised:

Medical Board Approval: