



Strengthen CMV Management for Your High-Risk Kidney Transplant Patients With Additional CMV Protection

CYTOGAM® (Cytomegalovirus Immune Globulin Intravenous [Human] [CMV-IGIV]) provides CMV-specific antibodies that complement antiviral therapy and may help protect your most vulnerable transplant recipients.¹⁻³

Late-onset CMV infection is a persistent and potent threat to kidney transplant patients, hitting hardest in high-risk (D+/R-) and at-risk patients who experience dosing or tolerability challenges from antivirals.⁴⁻¹⁰



Patients on belatacept immunosuppression^{4,6-8}



Patients facing challenges with delayed graft function (DGF)^{9,10}

Standard antiviral prophylaxis reduces CMV risk during therapy, but may leave a protection gap for these patients.⁵
CYTOGAM may help close this CMV vulnerability gap by offering additional protection.¹⁻³

CYTOGAM (CYTOMEGALOVIRUS IMMUNE GLOBULIN INTRAVENOUS [HUMAN])

CYTOGAM is an intravenous immunoglobulin containing standardized amount of antibody to cytomegalovirus.

INDICATION AND USAGE

It is indicated for the prophylaxis of cytomegalovirus disease associated with transplantation of kidney, lung, liver, pancreas and heart. In transplants of these organs other than kidney from CMV seropositive donors into seronegative recipients, prophylactic CMV-IGIV should be considered in combination with ganciclovir.

IMPORTANT SAFETY INFORMATION

CYTOGAM is contraindicated in individuals with a history of a prior severe reaction associated with the administration of this or other human immunoglobulin preparations. Persons with selective immunoglobulin A deficiency have the potential for developing antibodies to immunoglobulin A and could have anaphylactic reactions to subsequent administration of blood products that contain immunoglobulin A, including CYTOGAM.

Please see additional selected Important Safety Information throughout and full Prescribing Information enclosed in pocket.

Post-Prophylaxis: A Critical Window for CMV Vulnerability

Despite standard antiviral prophylaxis (6 months for kidney), CMV infection remains common in D+/R- recipients.⁵

After 6 months of antiviral prophylaxis with valganciclovir:

CMV infections still occurred in 38% (182/481) of patients⁵

CMV occurred in **38%**

median 264 days post-transplant
84 days after valganciclovir

A substantial portion of CMV infections occur months after prophylaxis, underscoring a persistent late-risk phase.⁵

49% CMV >3 mos

after valganciclovir

27% CMV >6 mos

after valganciclovir

IMPACT Trial: Even with extended antiviral prophylaxis (200 days vs 100 days), CMV infection remained an issue at 2 years in high-risk recipients.¹¹

21% at 2 years

after valganciclovir,
200 days

39% at 2 years

after valganciclovir,
100 days

IMPORTANT SAFETY INFORMATION FOR CYTOGAM (CONTINUED)

Immune Globulin Intravenous (Human) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Patients predisposed to acute renal failure include patients with any degree of preexisting renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Especially in such patients, IGIV products should be administered at the minimum concentrations available and the minimum rate of infusion practicable. Those containing sucrose as a stabilizer, like CYTOGAM, account for a disproportionate share of the total number of reports of renal dysfunction and acute renal failure when given at daily doses of 350 mg/kg or greater.

During administration, the patient's vital signs should be monitored continuously, and careful observation made for any symptoms throughout the infusion. Epinephrine and diphenhydramine should be available for the treatment of an acute and anaphylactic reactions.

Two Post-Transplant Populations Prone to Late, Invasive CMV

CMV risk is high for patients on belatacept immunosuppression and those with DGF.

CYTOGAM may add extra protection when patients are most vulnerable.

Patients on Belatacept

Patients on belatacept immunosuppression are at very high risk for developing severe, atypical CMV infections that may be tissue-invasive, prolonged, difficult to treat, and life-threatening.^{4,6,7}

6 months after conversion to belatacept immunosuppression⁷:

- Viral reactivation was more common than primary infection (prolonged)
- Most cases were tissue invasive (80% gastrointestinal, including 10% life-threatening cases)

Median time to CMV disease after transplant	29.5 months
>1 year to CMV disease after transplant	60% (24/40)
Primary infection	22.5% (9/40)
Viral reactivation	77.5% (31/40)
Tissue invasive; life-threatening	80% (32/40); 10% (4/40)

Patients with DGF

DGF patients have increased risk for CMV breakthrough infection during prophylaxis compared to non-DGF patients.^{8,10}

In 2 studies of kidney transplant patients with and without DGF^{9,10}

- CMV infection incidence was significantly higher for DGF patients in both studies^{9,10}
- Time to CMV infection was shorter in DGF patients¹⁰

	DGF patient	Non-DGF patient	P value
Study 1: CMV infection incidence ^{9*}	77.8% (21/31)	55.6% (79/160)	P=.032
Study 2: CMV infection incidence ^{10*}	22.8% (13/57)	11.3% (37/327)	P=.017
Time to CMV infection ¹⁰	143 days	298 days	P=.008

*Study designs differed.

IMPORTANT SAFETY INFORMATION FOR CYTOGAM (CONTINUED)

Increases in serum creatinine and blood urea nitrogen (BUN) have been observed as soon as one to two days following IGIV infusion. Progression to oliguria or anuria requiring dialysis has been observed.

Immune Globulin Intravenous (Human) products can contain blood group antibodies which may act as hemolysins and induce in vivo coating of red blood cells with immunoglobulin, causing a positive direct antiglobulin reaction and, rarely, hemolysis.

Please see additional selected Important Safety Information throughout and full Prescribing Information enclosed in pocket.

 **CYTOGAM**[®]
Cytomegalovirus Immune Globulin
Intravenous (Human) (CMV-IVIG)

Late-Onset CMV Remains a Significant Threat Despite Standard Prophylaxis

Certain patient groups—D+/R– recipients, belatacept-treated patients, and those with DGF—face especially elevated CMV risk^{5,7-10}

CYTOGAM® (Cytomegalovirus Immune Globulin Intravenous [Human] [CMV-IGIV]) offers a complementary mechanism of action to address the CMV protection gap¹⁻³

Scan the QR code to understand the CYTOGAM Mechanism of Action



IMPORTANT SAFETY INFORMATION FOR CYTOGAM (CONTINUED)

Thrombotic events have been reported in association with IGIV. Patients at risk may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, and/or known or suspected hyperviscosity. The potential risks and benefits of IGIV should be weighed against those of alternative therapies for all patients for whom IGIV administration is being considered. Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies.

CYTOGAM is derived from human plasma. As with all plasma-derived products, the risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

Minor reactions, such as flushing, chills, muscle cramps, back pain, fever, nausea, vomiting, arthralgia, and wheezing, were the most frequent adverse reactions observed during the clinical trials for CYTOGAM.

Please see full Prescribing Information in the pocket for full prescribing details.

To report SUSPECTED ADVERSE REACTIONS, contact Kamada at pharmacovigilance@kamada.com or 1-(866)-916-0077 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

References: 1. Pelletier JPR, Faisal Mukhtar F. Passive monoclonal and polyclonal antibody therapies. In: *Immunologic Concepts in Transfusion Medicine*. Elsevier Health. 2020;16:251-348. 2. Grossi P, Mohacsi P, Szabolcs Z, Potena L. Cytomegalovirus immunoglobulin after thoracic transplantation: an overview. *Transplantation*. 2016;100(Suppl 3):S1-S4. doi:10.1097/TP.0000000000001094 3. Carbone J. The immunology of posttransplant CMV infection: potential effect of CMV immunoglobulins on distinct components of the immune response to CMV. *Transplantation*. 2016;100(Suppl 3):S11-S18. doi:10.1097/TP.0000000000001095 4. Campbell A, Pruett TL. Revisiting the biological rationale for cytomegalovirus immune globulin (CMVIG) in the modern era of solid organ transplantation: current state and future direction. *Transplant Proc*. 2025;57(8):1610-1620. doi:10.1016/j.transproceed.2025.08.010 5. Rähä J, Ortiz F, Mannonen L, et al. The burden of cytomegalovirus infection remains high in high-risk kidney transplant recipients despite six-month valganciclovir prophylaxis. *Transpl Infect Dis*. 2021;23(4):e13577. doi:10.1111/tid.13577 6. Bertrand D, Chavarot N, Gatault P, et al. Opportunistic infections after conversion to belatacept in kidney transplantation. *Nephrol Dial Transplant*. 2020;35(2):336-345. doi:10.1093/ndt/gfz255 7. Chavarot N, Divard G, Scemla A, et al. Increased incidence and unusual presentations of CMV disease in kidney transplant recipients after conversion to belatacept. *Am J Transplant*. 2021;21(7):2448-2458. doi:10.1111/ajt.16430 8. Kleinherenbrink W, Baas M, Nakhsbandi G, et al. Delayed graft function and rejection are risk factors for cytomegalovirus breakthrough infection in kidney transplant recipients. *Pharmacol Res*. 2021;167:105565. doi:10.1016/j.phrs.2021.105565 9. Seo CH, Ju JJ, Kim MH, et al. Risk factors and long-term outcomes of delayed graft function in deceased donor renal transplantation. *Ann Surg Treat Res*. 2015;89(4):208-214. doi:10.4174/astr.2015.89.4.208 10. Shahmirzadi MR, Gunaratnam L, Jevnikar AM, et al. The effect of late-onset CMV infection on the outcome of renal allograft considering initial graft function. *Transpl Infect Dis*. 2023;25(4):e14081. doi:10.1111/tid.14081 11. Humar A, Limaye AP, Blumberg EA, et al. Extended valganciclovir prophylaxis in D+/R– kidney transplant recipients is associated with long-term reduction in cytomegalovirus disease: two-year results of the IMPACT study. *Transplantation*. 2010;90(12):1427-1431. doi:10.1097/tp.0b013e3181ff1493