FARMACI CON USO CONSOLIDATO NEL TRATTAMENTO CORRELATO AI TRAPIANTI PER INDICAZIONI ANCHE DIFFERENTI DA QUELLE PREVISTE DAL PROVVEDIMENTO DI AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
Basiliximab	**Profilassi del rigetto acuto in pazienti adulti e pediatrici sottoposti a trapianto di fegato e a trapianto isole di Langerhans.** **Profilassi del rigetto acuto in pazienti adulti sottoposti a trapianto di rene e pancreas.** M. Spada et al. Randomized Trial of Basixilimab Induction versus steroid Therapy in Pediatric Liver Allograft Recipients Under Tacrolimus Immunosuppression Am. J. Transplantation 2006; 6: 1913-1921. S. Gruttadauria et al. A Safe Immunosuppressive Protocol in Adult to-Adult Living Related Liver Transplantation. Transplant Proc 38, 1106-1108 (2006). Laura Lladò et al. Immunosuppression without steroids in liver transplantation is safe and reduces infection and metabolic complications: Results from a prospective multicenter randomized study. J. Hepatol 44 /(2006) 710-718. D.W. Orr et al. Anti-Interleukin 2 Receptor Antibodies and Mycorphenolate Mofetil for Treatment of Steroid - Resistant Rejection in Adult Liver Transplantation. Transplant Proc 37, 4373-4379 (2005). R. Ganschow et al. Long.-tern results of basixilimab induction immunosuppression in paediatric liver transplants recipients. Pediatr Transplantation 2005; 9: 741-745 M. Spada et al. An anti-interleukin 2 receptor monoclonal antibody to reduce the incidence of acute cellular rejection afetr liver transplantation. Pediatr Transplantation 2000, Vol 4., p. 62 (Abs P49). R. Ganschow et al. The anti-interleukin 2 receptor antodoby basixilimavb after pediatric liver transplantation: a pilot study. Pediatr Transplantation 2000, Vol. 4, p. 95 (Abs O145). R: Ganschow et al. First experience with basixilimab in pediatric liver graft recipients. Pediatr Transplantation 2001, Vol. 5, p. 353-358.

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	F. Filipponi et al. Study of Simulect.Based, Steroid-Free Immunosuppressive Regimen in HCV+ De Novo Liver Transplant Patients: Preliminary Results. Transplantation Proceedings 33, 3211-3212 (2001). D.A. Kelly The use of anti-interleukin 2 receptor antibodies in pediatric liver transplantation. Pediatr Transplantation 2001; 5: 386-389. P. Neuhaus et al. Improved Treatment Response With Basixilimab Immunoproflaxis Afetr Liver Transplantation: Results from a Double-Blind Randomized Placebo-Controlled Trial. Liver Transplantation 2002, Vol. 8, 132-142. M. Cantarovich et al. Anti-CD25 Mmonoclonal antibody coverage allows for calcuneurin inhibitor "Holiday" in solid organ transplant patients with acute renal dysfunction. Transplantation Vol 73 n 7. B. Nashan. The Interleukin " "Pathway" and the Route to Logical Immunosuppression. Current Issues in Liver and Small Bowel Transplantation 2002, 9, 164-174. E. Kuse et al. Immunoprophylaxis with Simulect ® (Basixilimab) in combination with Cyclosporine and Steoirds in Liver Transplantation. American Journal of Transplantation 2001, vol 1, p 202 (Abs 266). A. Venze et al. Basixilimab monotherpy following B-cell lymphoma after pediatric liver transplantation and anti- CD20 therapy. Pediatr Transplantation 2003; 7: 404-407. R. Reding et al. Stepird-free liver transplantation in children. Lancet 2003; 362: 2068-70. C.L. Liu et al. Interleukin 2-Receptor Antibody (Basiliximab) for Immunosuppressive Indcution Therapy Afer Liver Transplantation: A Protocol With Early Elimination of Seroids and Reduction of Tacrolimus Dosage. Liver Transplantation, 10: No. 6 (June) 728-733. S. Grattadauria et al. Basixilimab in a Triple-Drug Regiment with Tacrolimus and Steroids in Liver Transplantation. Transplantation Proceedings, 37, 2611-2613 (2005). <u>Trapianto di isole di Langerhans</u> Oberholzer J, Toso C, Triponez F, Ris F, Bucher P, et al:Human islet allotransplantation with Basiliximab in type I diabetic patients with end-stage renal failure. Transplantation Proceedings, 34, (3) 823-825

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Trapianto di Rene-Pancreas Zhang R, Florman S, Devidoss S, Zarifian A, Yau CL, Paramesh A, Killackey M, Alper B, Fonseca V, Slakey D. A comparison of long-term survivals of simultaneous pancreas-kidney transplant between African American and Caucasian recipients with basiliximab induction therapy. Am J Transplant. 2007 Jul;7(7):1815-21. Boggi U, Vistoli F, Del Chiaro M, Signori S, Amorese G, Vahadia Bartolo T, Sgambelluri F, Barsotti M, Tregnaghi C, Paleologo G, Coppelli A, Giannarelli R, Rizzo G, Marchetti P, Mosca F. Neoral versus prograf in simultaneous pancreas-kidney transplantation with portal venous drainage: three-year results of a single-center, open-label, prospective, randomized pilot study. Transplant Proc. 2005 Jul-Aug;37(6):2641-3. Chow FY, Polkinghorne K, Saunder A, Kerr PG, Atkins RC, Chadban SJ. Historical controlled trial of OKT3 versus basiliximab induction therapy in simultaneous pancreas-renal transplantation. Nephrology (Carlton). 2003 Aug;8(4):212-6. **Profilassi del rigetto acuto in pazienti adulti e pediatrici sottoposti a trapianto di cuore.** Trapianto di cuore J. Segovia et al A randomized Multicenter Comparison of Basiliximab and Muromonab (OKT3) in Heart Transplantation: SIMCOR Study . Transplantation 2006; 81:1542-1548 F.M. Mattei et al. Lower Risk of Infectious Deaths in Cardiac Transplant Patients Receiving Basiliximab versus Anti-thymocyte Globulin as Induction Therapy J Heart Lung Transplantation 2007; 26:693-9 Katrina A. Ford et al. Initial Data on Basiliximab in Critically Children Undergoing Heart Transplantation J Heart Lung Transplantation 2005; 24:1284-88 K.M. Ward et al. Basiliximab in pediatric heart transplantation-Initial Experience J Heart Lung Transplantation 2004; Abs 103 – Vol 23 – Number 2S **Terapia immunodepressiva e antirigetto in pazienti adulti e pediatrici sottoposti a tx di intestino e multi-viscerale.**

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Adenovirus Infections in Pediatric Small Bowel Transplant Recipients, Diana F. Florescu, Monirul K. Islam, David F. Mercer, Wendy Grant, Alan N. Langnas, Alison G. Freifeld, Debra Sudan, Rishika Basappa, Dominick Dimaio, and Andre C. Kalil, Transplantation 2010;90: 198–204 Graft-vs-host disease after small bowel transplantation in children, Ane M. Andres, Manuel Lopez Santamaría, Esther Ramos, Jesus Sarriá, Manuel Molina, Francisco Hernandez, Jose L. Encinas, Javier Larrauri, Gerardo Prieto, Juan Antonio Tovar, Department of Pediatric Surgery, Hospital Universitario La Paz, Paseo de la Castellana 261, 28046 Madrid, Spain, 27 October 2009, Journal of Pediatric Surgery (2010) 45, 330–336 Basiliximab Decreases the Incidence of Acute Rejection After Intestinal Transplantation, D.L. Sudan, S. Chinnakotla, S. Horslen, K. Iyer, I. Fox, B. Shaw Jr, and A.N. Langnas, Transplantation Proceedings, 34, 940–941 (2002) Incidence and outcome of fungal infections in pediatric small bowel transplant recipients, D.F. Florescu, K.M. Islam,W. Grant, D.F. Mercer, A. Langnas, J. Botha, B. Nielsen, A.C. Kalil, Transpl Infect Dis 2010, 1-8. Graft-versus-Host Disease Presenting With Pancytopenia After En Bloc Multiorgan Transplantation: Case Report and Literature Review, R. Mawad, A. Hsieh, and L. Damon, Transplantation Proceedings, 41, 4431–4433 (2009). Intestinal transplantation before and after the introduction of sirolimus Thomas M. Fishbein, Sander Florman, Gabriel Gondolesi, Thomas Schiano, Neal Leleiko, Allan Tschernia, and Stuart Kaufman, Transplantation, Vol. 73, 1538–1542, No. 10, May 27, 2002. **In associazione con ciclosporina, micofenolato mofetile e metrotressato, per la profilassi della aGVHD in pazienti sottoposti a trapianto allogenico di cellule staminali ematopoietiche non manipolate da donatore familiare HLA aploidentico refrattari alla terapia con corticosteroidi.** Humanized anti-CD25 monoclonal antibody for prophylaxis of graft-versus-host disease (GVHD) in haploidentical bone marrow transplantation without ex vivo T-cell depletion. Chen HR, Ji SQ, Wang HX et al. Exp Hematol 2003; 31:1019-1025. Anti-CD25 monoclonal antibody (basiliximab) for prevention of graft-versus-host disease after haploidentical bone marrow transplantation for hematological malignancies. Ji SQ, Chen HR, Yan HX et al. Bone Marrow Transplantation 2005; 36:349-354.

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Haploidentical hematopoietic stem cell transplantation in hematologic malignanices with G-CSF mobilize bone marrow plus peripheral blood stem cells grafts without T cell depleted: a single center report of 29 cases. Wang HX, Yan HM, Wang ZD et al. Leukemia & Lymphoma 2012; 53:654-659. Prophylaxis of graft-versus-host disease by administration of the murine anti-IL-2 receptor antibody 2A3. Anasetti C, Martin PJ, Storb R et al. Bone Marrow Transplant 1991; :375-381. Comparative in vitro study of the immunomodulatory activity of humanized and chimeric anti-CD25 monoclonal antibodies. Kircher B, Lätzer K, Gastl G and Nachbaur D. Clin Exp Immunol 2003; 134:426-430. Prophylactic effects of interleukin-2 receptor antagonists against graft-versus-host disease following unrelated donor peripheral blood stem cell transplantation. Fang J, Hu C, Hong M et al. Biol Blood Marrow transplant 2012; 18:745-762. Haploidentical, unmanipulated, G-CSF-primed bone marrow transplantation for patients with high-risk hematologic malignancies. Di Bartolomeo P, Santarone S, De Angelis G et al. Blood 2012; 121:849-857.
Everolimus 0,25/0,5/0,75/1mg	**Profilassi del rigetto acuto in pazienti pediatrici sottoposti a trapianto di rene.** **Profilassi del rigetto acuto in pazienti adulti sottoposti a trapianto di polmone.** **Pazienti con trapianto di fegato che necessitano la riduzione/sospensione nell'inibitore della calcineurina con problemi di tossicità renale.** L.Pape et al. Reversal of loss of glomerular fuiltration rate in children with transplant nephropathy after switch to everolimus and low-dose cyclosporine A. Pediatr Transplantation 2007: 11: 291-293 Vester U et al. Everolimus (Certican) in combination with Neoral in Pediatric Renal Transplant Recipients: Interim analysis after 3 Months. Transplantattion Proceedings, 34, 2209-2210 (2002) P. Hoyer et al. Everolimus in Pediatric de Novo Renal Transplant Patients. Transplantation Vol 75; 2082-2085 (2003) R. Van Damme-Lombaerts et al. Single-dose pharmacokinetics and tolerability of everolimus in stable pediatric renal transplant patients. Pediatric Transplantation 2002; 6: 147-152

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	J.M. Kovarik et al. Everolimus in Pulmonary Transplantation: Pharmacokinetics and Exposure-Response Relationship. The Journal of Heart and Lung Transplantation Vol. 25 No 4 (2006) Everolimus versus Azathioptine in Maintenance Lung Transplant Recipients: An International, Randomized Double-Blind Clinical Trial. American Journal of Transplantation 2006; 6: 169-177 Azzola et al. Everolimus and Mycophenolate Mofetil are poten inhibitors of fibroblast proliferation after lung Transplantation. Transplantation Vol 77, No. 4 (2004) G. Everson. Everolmus and mTOR Inhibitors in Liver Transplantation: Opening the "Box". Liver Transplantation 12: 1571-1573, 2006 C.D. Poirier Promise of Neoarl C2; Basixilimab and Everolumus in Lung Transplantation. Transplantation Proceedings, 36 (Suppl 2S)N, 509S-513S (2004) Levy e al. Safety, Telerability and Efficacy of Everolimus in De Novo Liver Transplant Recipients: 12-and 36-Month Results. Liver Transplantation 12: 1640-1648, 2006 **Trapianto di fegato pediatrico** Katrina A. Ford Paediatric Immunosuppression Following Solid Organ Transplantation Arch Dis Child Educ Ed 2006; 91:87-91 **Terapia immunodepressiva e antirigetto in pazienti adulti e pediatrici sottoposti a tx di intestino e multi-viscerale.** Persistent effects of everolimus on strength of experimental wounds in intestine and fascia, Martine C. M. Willems, MD1; J. Adam van der Vliet, MD, PhD1; Ben M. de Man, BSc1; Jeroen A. W. M. van der Laak, PhD2; Roger M. L. M. Lomme, BSc1; Thijs Hendriks, PhD1, Wound Rep Reg (2010) 18; 98–104

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Fattori di crescita dei leucociti: • **filgrastim** • **lenograstim**	**Neutropenia (neutrofili < 750/L) nei pazienti trapiantati di fegato o con diagnosi clinica di cirrosi, che presentano risposta virologica precoce alla terapia**. Manns MP, et al. and the International Hepatitis Interventional Therapy Group. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. Lancet 2001;358:958-65. Fried MW, et al. Peg Interferon alf 2a plus Ribavirin in chronic hepatitis C virus infection. N Engl J Med 2002; 347: 975-82. Higashi Y, et al. Case report: agranulocytosis induced by inteferon alpha therapy for chronic hepatitis C J Gastroenterol Hepatol 1996; 11:1012-1015. Van Thiel DH, et al. Combination treatment of advanced HCV associated liver disease with interferon and G-CSF. Hepatogastroenterology 1995; 42:907-12 Fukuda A, et al. Effects of interferon alpha on peripheral neutrophil counts and serum granulocyte colony-stimulating factor for the treatment of chronic hepatitis C Cell Mol Ther 2000; 6:149-154. Carreno V, et al. Randomized controlled trial of recombinant human granulocyte-macrophage colony-stimulating factor for the treatment of chronic hepatitis C Cytokine 2000; 12: 165-70. Shiffman ML, et al. Use of granulocyte macrophage colony stimulating factor alone or in combination with interferon-alpha-2b for treatment of chronic hepatitis C J Hepatol 1998; 28: 382-89. National Institutes of health consensus development conference statement: Management of hepatitis C: 2002 – June 10-12 2002. Hepatology 2002; 36: S3-S20. **Neutropenia nei pazienti trapiantati di rene** Hurst FP et al. Poor outcomes associated with neutropenia after kidney transplantation: analysis of United States Renal Data System. Transplantation. 2011 Jul 15;92(1):36-40. Zafrani L, et al. Incidence, risk factors and clinical consequences of neutropenia following kidney transplantation: a

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	retrospective study. Am J Transplant. 2009;9(8):1816-25.
Fotemustina (e.v.)	**In sostituzione della carmustina nel condizionamento BEAM**. Musso M. et al., Bone Marrow Transplantation 2009 November 1-7.
Immunoglobulina di coniglio antitimocitaria	**Trattamento e profilassi della malattia acuta e cronica da trapianto verso ospite (Graft versus Host Disease, GvHD) nei pazienti adulti refrattari alla terapia di I linea con corticosteroidi** **Profilassi e trattamento della malattia acuta e cronica da trapianto verso ospite (Graft versus Host Disease, GvHD) nei pazienti pediatrici refrattari alla terapia di I linea con corticosteroidi** **Regime di condizionamento nel trapianto autologo per malattie autoimmuni** Use of antithymocyte globulin for treatment of steroid-refractory acute graft-versus-host disease: an international practice survey B Hsu, R May, G Carrum, R Krance and D Przepiorka Bone Marrow Transplantation (2001) 28, 945–950. Treatment of acute graft-versus-host disease with low-dose, alternate-day antithymocyte globulin Francesco Graziani, Maria Teresa Van Lint, Alida Dominietto, Anna Maria Raiola, Carmela Di Grazia, Teresa Lamparelli, Francesca Gualandi, Stefania Bregante, Merilù Fiorone, Barbara Bruno, Andrea Bacigalupo haematologica 2002; 87:973-978. Fludarabine, cyclophosphamide and anti-thymocyte globulin for alternative donor transplants in acquired severe aplastic anemia: a report from the EBMT-SAA Working Party. A Bacigalupo, F Locatelli, E Lanino, J Marsh, G Socie´, S Maury, A Prete, A Locasciulli, S Cesaro and J Passweg, for the Severe Aplastic Anemia Working Party of the European Group for Bloodand Marrow Transplantation (SAA WP-EBMT) Bone Marrow Transplantation (2005) 36, 947–950. Fludarabine, cyclophosphamide plus thymoglobulin conditioning regimen for unrelated bone marrow transplantation in severe aplastic anemia HJ Kang, HY Shin, HS Choi and HS Ahn. Bone Marrow Transplantation (2004) 34, 939–943. Reduced intensity conditioning using intravenous busulfan, fludarabine and rabbit ATG for children with nonmalignant

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	disorders and CML. B Horn, L-A Baxter-Lowe, L Englert, A McMillan, M Quinn, K DeSantes and M Cowan. Bone Marrow Transplantation (2006) 37, 263–269. Nonmyeloablative stem cell transplantation for nonmalignant diseases in children with severe organ dysfunction A Kikuta, M Ito, K Mochizuki, M Akaihata, K Nemoto, H Sano and H Ohto. Bone Marrow Transplantation (2006) 38, 665–669. Use of antithymocyte globulin for treatment of steroid-refractory acute graft-versus-host disease: an international practice survey. B Hsu, R May, G Carrum, R Krance and D Przepiorka. Bone Marrow Transplantation (2001) 28, 945–950. Favourable response to antithymocyte globulin therapy in resistant acute graft-versus-host disease.A. Tagliabue, P. Corti, E Vigano`, S. Bonanomi, C. Uderzo. Bone Marrow Transplantation (2005) 36, 45. Once-Daily Intravenous Busulfan Given with Fludarabine as Conditioning for Allogeneic Stem Cell transplantation: Study of Pharmacokinetics and Early Clinical Outcomes.J. A. Russell, H. T. Tran, D. Quinlan, A. Chaudhry, P. Duggan, C. Brown, D. Stewart, J. D. Ruether, D. Morris, S. Glück, E. Gyonyor, B. S. Andersson Biology of Blood and Marrow Transplantation 8:468-476 (2002). Graft-versus-host disease following allogeneic transplantation from HLA-identical sibling with antithymocyte globulin–based reduced-intensity preparative regimen. Mohamad Mohty, Jacques-Olivier Bay, Catherine Faucher, Bachra Choufi, Karin Bilger, Olivier Tournilhac, Norbert Vey, Anne-Marie Stoppa, Diane Coso, Christian Chabannon, Patrice Viens, Dominique Maraninchi, and Didier Blaise. Blood, 15 July 2003 - Vol 102, Number 2. Antithymocyte globulin affects the occurrence of acute and chronic graft-versus-host disease after a reduced-intensity conditioning regimen by modulating mixed chimerism induction and immune reconstitution. Nakai K, Mineishi S, Kami M, Saito T, Hori A, Kojima R, Imataki O, Hamaki T, Yoshihara S, Ohnishi M, Kim SW, Ando T, Fumitoh A, Kanda Y, Makimoto A, Tanosaki R, Kanai S, Heike Y, Ohnishi T, Kawano Y, Wakasugi H, Takaue Y. Transplantation 2003 Jun 27;75(12):2135-43 Reduced-intensity preparative regimen and allogeneic stem cell transplantation for advanced solid tumors. Blaise D, Bay JO, Faucher C, Michallet M, Boiron JM, Choufi B, Cahn JY, Gratecos N, Sotto JJ, François S, Fleury J, Mohty M, Chabannon C, Bilger K, Gravis G, Viret F, Braud AC, Bardou VJ, Maraninchi D, Viens P. Blood 2004 Jan 15;103(2):435-41. Protective Conditioning for Acute Graft-versus-Host Disease. Robert Lowsky, M.D., Tsuyoshi Takahashi, M.D., Ph.D., Yin Ping Liu, M.D., Sussan Dejbakhsh-Jones, M.S., F. Carl Grumet, M.D., Judith A. Shizuru, M.D., Ph.D., Ginna G. Laport, M.D., Keith E. Stockerl-Goldstein, M.D., Laura J. Johnston, M.D., Richard T. Hoppe, M.D., Daniel A. Bloch, Ph.D., Karl G. Blume, M.D., Robert

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	S. Negrin, M.D., and Samuel Strober, M.D. N Engl J Med Sept 29, 2005 353;13. Reduced Incidence of Acute and Chronic Graftversus-Host Disease with the Addition of Thymoglobulin to a Targeted Busulfan/Cyclophosphamide Regimen. H. Joachim Deeg, Barry E. Storer, Michael Boeckh, Paul J. Martin, Jeannine S. McCune, David Myerson, Shelly Heimfeld, Mary E. Flowers, Claudio Anasetti, Kristine C. Doney, John A. Hansen, Hans-Peter Kiem, Richard A. Nash, Paul V. O'Donnell, Jerald P. Radich, Brenda M. Sandmaier, Bart L. Scott, Mohamed L. Sorror, E. Houston Warren, Robert P. Witherspoon, Ann Woolfrey, Frederick R. Appelbaum, Rainer Storb. Biology of Blood and Marrow Transplantation 12:573-584 (2006). Allogeneic transplantation for adult acute leukemia in first and second remission with a novel regimen incorporating daily intravenous busulfan, fludarabine, 400 CGY total-body irradiation, and Thymoglobulin. Russell JA, Savoie ML, Balogh A, Turner AR, Larratt L, Chaudhry MA, Storek J, Bahlis NJ, Brown CB, Quinlan D, Geddes M, Stewart DA. Biol Blood Marrow Transplant. 2007 Jul;13(7):814-21. Adult Recipients of Matched Related Donor Blood Cell Transplants Given Myeloablative Regimens Including Pretransplant Antithymocyte Globulin Have Lower Mortality Related to Graft-versus-Host Disease: A Matched Pair Analysis. James A. Russell, A. Robert Turner, Loree Larratt, Ahsan Chaudhry, Donald Morris, Christopher Brown,1,2 Diana Quinlan, Douglas Stewart. Biology of Blood and Marrow Transplantation 13:299-306 (2007). Autologous hematopoietic stem cell transplantation for autoimmune diseases: an observational study on 12 years' experience from the European Group for Blood and Marrow Transplantation Working Party on Autoimmune Diseases.Farge D, Labopin M, Tyndall A, Fassas A, Mancardi GL, Van Laar J, Ouyang J, Kozak T, Moore J, Kötter I, Chesnel V, Marmont A, Gratwohl A, Saccardi R. Haematologica. 2010 Feb;95(2):284-92 Autologous stem cell transplantation for progressive multiple sclerosis: update of the European Group for Blood and Marrow Transplantation autoimmune diseases working party database. Saccardi R, Kozak T, Bocelli-Tyndall C, Fassas A, Kazis A, Havrdova E, Carreras E, Saiz A, Löwenberg B, te Boekhorst PA, Gualandio F, Openshaw H, Longo G, Pagliai F, Massacesi L, Deconink E, Ouyang J, Nagore FJ, Besalduch J, Lisukov IA, Bonini A, Merelli E, Slavino S, Gratwohl A, Passweg J, Tyndall A, Steck AJ, Andolina M, Capobianco M, Martin JL, Lugaresi A, Meucci G, Sáez RA, Clark RE, Fernandez MN, Fouillard L, Herstenstein B, Koza V, Cocco E, Baurmann H, Mancardi GL; Autoimmune Diseases Working Party of EBMT. Mult Scler. 2006 Dec;12(6):814-23. Haematopoietic SCT in severe autoimmune diseases: updated guidelines of the European Group for Blood and Marrow Transplantation. Snowden JA, Saccardi R, Allez M, Ardizzone S, Arnold R, Cervera R, Denton C, Hawkey C, Labopin M,

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Mancardi G, Martin R, Moore JJ, Passweg J, Peters C, Rabusin M, Rovira M, van Laar JM, Farge D; EBMT Autoimmune Disease Working Party (ADWP); Paediatric Diseases Working Party (PDWP). Bone Marrow Transplant. 2012 Jun;47(6):770-90 **Profilassi degli episodi di rigetto acuto dopo trapianto di polmone in soggetti con fibrosi cistica** Jaksch P, et al. Antithymocyte globulin induction therapy improves survival in lung transplantation for cystic fibrosis. Transpl Int. 2013 Jan;26(1):34-41.
Micofenolato Mofetile	**Trapianto cuore pediatrico** **Trapianto fegato pediatrico** **Trapianto pancreas** **Trapianto polmone** **Trapianto isole di Langerhans** **Profilassi e trattamento della GVHD nel trapianto di cellule staminali emopoietiche nei pazienti refrattari alla terapia di I linea con corticosteroidi** <u>Trapianto di cuore pediatrico</u> J. Agüero et al. Influence of Immunosuppression Regimen on Heart Transplantation Survival. Transplantation Proceedings 2006; 38: 2550–2 Olivia Boyer et al. Improvement of Renal Function in Pediatric Heart Transplant Recipients Treated with Low-Dose Calcineurin Inhibitor and Mycophenolate Mofetil. Transplantation 2005; 79 (10): 1405–1410 Dipchand AI et al. Mycophenolate mofetil in pediatric heart transplant recipients: A single-center experience. Pediatr Transplantation 2001: 5: 112–118. Tonshoff B et al. Treatment strategies in pediatric solid organ transplant recipients with calcineurin inhibitor-induced nephrotoxicity. Pediatr Transplantation 2006; 10: 721–729. Groetzner J et al. Cardiac transplantation in pediatric patients: fifteen-year experience of a single center. Ann Thorac Surg 2005; 79 (1): 53-60. Since the introduction of mycophenolate mofetil, freedom from acute rejection increased to 62%. Gajarski RJ et al. Lack of correlation between MMF dose and MPA level in pediatric and young adult cardiac transplant

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	patients: does the MPA level matter? Am J Transplant 2004; 4 (9): 1495-500 Shaddy RE et al. Mycophenolic mofetil reduces the HLA antibody response of children to valved allograft implantation. Ann-Thorac-Surg 2004; 77 (5): 1734-9 This study demonstrates the ability to pharmacologically abrogate the HLA class I antibody response to valved allograft implantation in children using MMF. Boucek RJ, Boucek MM Pediatric heart transplantation. Curr-Opin-Pediatr 2002; 14 (5): 611-9 Currently, recipients are maintained on immunosuppressive medications that target calcineurin (eg, cyclosporine, tacrolimus), lymphocyte proliferation (eg, azathioprine, mycophenolate mofetil (MMF), sirolimus) and, in some instances antiinflammatory corticosteroids. Kobashigawa Review of Major Clinical Trials with Mycophenolate Mofetil in Cardiac Transplantation. Transplantation 2005; 80 (2S): S235–S243. <u>Trapianto di fegato pediatrico</u> Renz JF et al. Mycophenolate mofetil, microemulsion cyclosporine, and prednisone as primary immunosuppression for pediatric liver transplant recipients. Liver Transpl Surg. 19995(2): 136-43 Chardot C et al. Use of mycophenolate mofetil as rescue therapy after pediatric liver transplantation. Transplantation 2001; 71 (2): 224-9. These preliminary results suggest that MMF is an effective and safe immunosuppressant in pediatric LT recipients. Its use is hampered by frequent gastrointestinal and hematological side-effects. MMF does not seem to increase the risk of PTLD nor CMV disease. Aw MM et al. Calcineurin-inhibitor related nephrotoxicity- reversibility in paediatric liver transplant recipients. Transplantation 2001; 72 (4): 746-9. MMF allows the recovery of renal function from CI related nephrotoxicity in more than 70% of paediatric liver transplant recipients with renal impairment. Ferraris JR et al. Mycophenolate mofetil and reduced doses of cyclosporine in pediatric liver transplantation with chronic renal dysfunction: changes in the immune responses. Pediatr Transplant 2004; 8 (5): 454. Evans HM et al. Mycophenolate Mofetil for Renal Dysfunction after Pediatric Liver Transplantation. Transplantation 2005; 79: 1575–1580) Klupp J et al. Indications of Mycophenolate Mofetil in Liver Transplantation. Transplantation 2005; 80: S142–S146. Marion M. Mycophenolic Acid Pharmacokinetics in Pediatric Liver Transplant Recipients. Liver Transplantation 2003; 9 (4):

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	383-388. Apezzato ML et al. Mycophenolate mofetil promotes prolonged improvement of renal dysfunction after pediatric liver transplantation: Experience of a single center. Pediatr Transplantation 2007: 11: 82–86. Tredger JM. Monitoring Mycophenolate in Liver Transplant Recipients: Toward a Therapeutic Range. Liver Transplantation 2004; 10 (4): 492–502. Mention K et al. Renal function outcome in pediatric liver transplant recipients. Pediatr-Transplant 2005; 9 (2): 201-7 Nobili V et al. Mycophenolate mofetil in pediatric liver transplant patients with renal dysfunction: preliminary data. Pediatr-Transplant 2003; 7 (6): 454-7 . <u>Trapianto di Pancreas</u> Odorico JS et al. Improved solitary pancreas transplant graft survival in the modern immunosuppressive era. Cell-Transplant 2000; 9 (6): 919-27. Rigotti P et al. Mycophenolate mofetil (MMF) versus azathioprine (AZA) in pancreas transplantation: a single-center experience. Clin-Nephrol 2000; 53 (4): 52-4. In conclusion, patients treated with MMF required less frequent and less intensive treatment for acute rejection. However, its short- and long-term side effects should be further investigated. Gruessner RW et al. Mycophenolate mofetil in pancreas transplantation. Transplantation 1998; 66 (3): 318-23. For SPK recipients, the incidence of acute reversible rejection episodes was significantly lower with MMF than with azathioprine. Paleologo G et al. Solitary pancreas transplantation: preliminary findings about early reduction of proteinuria in incipient or evident diabetic type I nephropathy. Transplant Proc 2004; 36 (3): 591-6 The immunosuppressive therapy used basilixmab induction and tacrolimus, mycophenolate mophetil (MMF), and low dose steroid maintenance therapy. Kaufman DB et al. Pancreas transplantation at Northwestern University. Clin Transpl 2000; 239-46 We have found that multimodal immunotherapy including induction with tacrolimus-based maintenance combined with either MMF or sirolimus, with or without corticosteroids, resulted in excellent patient and graft survival rates with low rates of rejection. Sutherland DE et al. Lessons learned from more than 1,000 pancreas transplants at a single institution. Ann Surg 2001; 233 (4): 463-501

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	From December 16, 1966, to March 31, 2000, the authors performed 1,194 pancreas transplants. The analyses were divided into five eras: era 0, 1966 to 1973 (n = 14), historical; era 1, 1978 to 1986 (n = 148), transition to cyclosporine for immunosuppression, multiple duct management techniques, and only solitary (PAK and PTA) transplants; era 2, 1986 to 1994 (n = 461), all categories (SPK, PAK, and PTA), predominantly bladder drainage for graft duct management, and primarily triple therapy (cyclosporine, azathioprine, and prednisone) for maintenance immunosuppression; era 3, 1994 to 1998 (n = 286), tacrolimus and mycophenolate mofetil used; and era 4, 1998 to 2000 (n = 275), use of daclizumab for induction immunosuppression, primarily enteric drainage for SPK transplants, pretransplant immunosuppression in candidates awaiting PTA Patient and graft survival rates have significantly improved over time as surgical techniques and immunosuppressive protocols have evolved. Jordan ML et al. Steroid withdrawal for pancreas transplants under tacrolimus immunosuppression. Transplant-Proc 2001; 33 (1-2): 1655. Egidi FM. Management of Hyperglycaemia After Pancreas Transplantation. Are New Immunosuppressants the Answer? Drugs 2005; 65 (2): 153-166. Garcia VD et al. Immunosuppression in Pancreas Transplantation: Mycophenolate Mofetil Versus Sirolimus. Transplantation Proceedings 2004; 36: 975–977. Gruessner AC, Sutherland DER. Pancreas transplant outcomes for United States (US) and non-US cases as reported to the United Network for Organ Sharing (UNOS) and the International Pancreas Transplant Registry (IPTR) as of June 2004. Clin Transplant 2005: 19: 433–455. Jung M et al. Comparison of Azathioprine and Mycophenolate Mofetil for the Prevention of Acute Rejection in Recipients of Pancreas Transplantation. J Clin Pharmacol 2001;41: 861-869. In conclusion, compared with AZA, MMF significantly reduces the rate of biopsy-proven pancreas rejection during the first 6 months of transplantation and is well tolerated,Mark W et al. Impact of Steroid Withdrawal on Metabolic Parameters in a Series of 112 Enteric/Systemic-Drained Pancreatic Transplants. Transplantation Proceedings 2005, 37, 1821–1825. <u>Trapianto di Polmone</u> Izbicki G et al. Improved Survival After Lung Transplantation in Patients Treated With Tacrolimus/Mycophenolate Mofetil as Compared With Cyclosporine/Azathioprine. Transplantation Proceedings 2002; 34: 3258–3259 Lama R et al. Lung Transplants With Tacrolimus and Mycophenolate Mofetil: A Review. Transplantation Proceedings 2003;

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	35: 1968–1973. Palmer SM et al. Results of a randomized, prospectiv, multicenter trial of Mycophenolate Mofetil versus azathioprine in the prevention of acute lung allograft rejection. Transplantation 2001; 71: 1772–1776. McNeil K et al. Comparison of Mycophenolate Mofetil and Azathioprine for Prevention of Bronchiolitis Obliterans Syndrome in De Novo Lung Transplant Recipients. Transplantation 2006; 81 (7): 998–1003. Roman A et al. Preliminary Results of Rescue Therapy With Tacrolimus and Mycophenolate Mofetil in Lung Transplanted Patients With Bronchiolitis Obliterans. Transplantation Proceedings 2002; 34: 146–147 Treede H et al. Tacrolimus versus Cyclosporine after Lung Transplantation: A Prospective, Open, Randomized Two-Center Trial Comparing Two Different Immunosuppressive Protocols. J Heart Lung Transplant 2001; 20: 511–517. Zuckermann A et al. Comparison Between Mycophenolate Mofetil and Azathioprine-Based Immunosuppressions in Clinical Lung Transplantation. J Heart Lung Transplant 1999;18: 432–440. Zuckermann A et al. Benefit of Mycophenolate Mofetil in Patients With Cyclosporine A-Induced Nephropathy After Lung Transplantation. Transplantation Proceedings 1999; 31: 1160–1161 Bhorade SM et al. Comparison of three tacrolimus-based immunosuppressive regimens in lung transplantation. Am J Transplant. 2003; 3 (12): 1570-5 Addition of daclizumab and MMF to a tacrolimus-based immunosuppressive regimen decreased the incidence of acute rejection episodes without increasing any adverse events in our lung transplantation population. Groetzner J et al. Conversion to sirolimus and mycophenolate can attenuate the progression of bronchiolitis obliterans syndrome and improves renal function after lung transplantation. Transplantation. 2006; 81 (3): 355-60. After BOS was diagnosed, conversion to MMF and Sir stabilized graft function only in some of the converted patients. Therefore, earlier administration of Sir-based immunosuppression might be a more promising approach. Whether conversion to CNI-free immunosuppression can actually ameliorate the extent or progression of BOS has to be investigated in randomized trials. <u>Trapianto di isole di Langerhans</u>

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Shapiro AMJ, Ricordi C, Hering BJ et al: International trial of the Edmonton Protocol for islet transplantation. N Engl J Med 2006; 355: 1318-30. Froud T, Baidal DA, Ponte G, Ferreira DV, Ricordi C, Alejandro R: Resolution of neurotoxicity and beta-cell toxicity in an islet transplant recipient following substitution of tacrolimus with MMF. Cell transplant 2006, 15 (7): 613-629 **Terapia immunodepressiva e antirigetto in pazienti adulti e pediatrici sottoposti a tx di intestino e multi-viscerale.** Mycophenolate Mofetil–Related Gastrointestinal Mucosal Injury in Multivisceral Transplantation V. Delacruz, D. Weppler, E. Island, M. Gonzalez, P. Tryphonopoulos, J. Moon, L. Smith, A. Tzakis, and P. Ruiz, Transplantation Proceedings, 42, 82–84 (2010) Intestinal transplantation: evolution in immunosuppression protocols, Jacques Pirenne and Masaru Kawai, Current Opinion in Organ Transplantation 2009, 14:250–255 Living-Related Small Bowel Transplantation for Three Patients With Short Gut Syndrome, M. Li, G. Ji, F. Feng, W. Song, R. Ling, D. Chen, X. Liu, J. Li, H. Shi, W. Wang, and H. Zhang, Transplantation Proceedings, 40, 3629–3633 (2008) Non-composite combined liver and intestinal allotransplantation, Ning Li, You-Sheng Li, Yuan-Xin Li, Wei-Ming Zhu, Xiao-Dong Ni, Liang Zhu, Bin Cao, Wei-Su Li, Kai Luo and Jie-Shou Li, Hepatobiliary Pancreat Dis Int 2006; 5: 613-616 Living Related Segmental Bowel Transplantation From Experimental to Standardized Procedure Enrico Benedetti, MD,* Mark Holterman, MD,† Massimo Asolati, MD,* Stefano Di Domenico, MD,* Jose´ Oberholzer, MD,* Howard Sankary, MD,* Herand Abcarian, MD,‡ and Giuliano Testa, MD*, Ann Surg 2006;244: 694–699 Isolated small bowel transplantation from a living-related donor at the Catholic University of Korea--a case report of rejection -free course-, Lee MD, Kim DG, Ahn ST, Moon IS, Choi MG, Hong SG, Park SC, Chung IS, Choi JY, Yoon SK, Kim SI, Choi JH, Jung ES, Yonsei Med J. 2004 Dec 31;45(6):1198-202. [A case report of simultaneous liver, pancreas-duodenum, and kidney transplantation in a patient with post-hepatitic cirrhosis combined with uremia and insulin-dependent diabetes related to chronic pancreatitis], Wang H, Dou KF, Yang XJ, Qin WJ, Zhang G, Yu L, Kang FX, Chen SY, Xiong LZ, Song ZS, Liu ZC, Zhonghua Yi Xue Za Zhi. 2006 Sep 12;86(34):2421-4. [Article in Chinese].

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Profilassi e terapia della GVHD acuta e cronica nel trapianto di cellule staminali emopoietiche (Midollo, Sangue periferico, Cordone Ombelicale) nei pazienti pediatrici refrattari alla terapia di I linea con corticosteroidi Haploidentical hematopoietic stem cell transplantation for the treatment of severe aplastic anemia in children. Liu Y, Tang SQ, Huang WR, Li HH, Zhao Y, Bo J, Zhang N, Wang F, Yu L.Department of Pediatrics, Chinese PLA General Hospital, Beijing 100853, China. Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2013 Jul;21(4):985-9. Impact of Graft-versus-Host Disease Prophylaxis on Outcomes after Myeloablative Single-Unit Umbilical Cord Blood Transplantation. Sanz J, Picardi A, Hernández Boluda JC, Martín C, Ferrá C, Nozzoli C, Gonzalez-Vicent M, Rambaldi A, Valcarcel D, Verdeguer A, Serrano D, de Heredia CD, Pascual MJ, de Paz R, Montesinos P, Bartolozzi B, Algarotti A, Sanz MA, Arcese W, Sanz GF; GETH and GITMO. Biol Blood Marrow Transplant. 2013 Sep;19(9):1387-92. Allogeneic stem cell transplantation for 8 patients with malignant infantile osteopetrosis in China. Zhu GH, Qin MQ, Wang B, Zhou X, Yang J, Jia CG, Wu Y, Wang XS, Wu MY. Zhonghua Er Ke Za Zhi. 2012 Nov;50(11):807-12. An age-dependent pharmacokinetic study of intravenous and oral mycophenolate mofetil in combination with tacrolimus for GVHD prophylaxis in pediatric allogeneic stem cell transplantation recipients. Bhatia M, Militano O, Jin Z, Figurski M, Shaw L, Moore V, Morris E, Tallamy B, van deVen C, Ayello J, et al. Biol Blood Marrow Transplant. 2010 Mar; 16(3):333-43.
Micofenolato Sodico	**Profilassi del rigetto acuto in pazienti adulti con trapianto di cuore.** **Pazienti adulti con trapianto di fegato e di cuore in cui il micofenolato mofetile dia effetti collaterali di tipo gastroenterico che richiedano la diminuzione/sospensione della dose.** J. Kobashigawa et al. Similar Efficacy and Safety of Enteric-coated Mycophenolate Sodium (E-MPS, Myfortic) compared with Mycophenolate Mofetil (NNF) in de Novo Transplant Recipients: Results of a 12-Month, Single-blind, Randomized, Parallel-Group, Multicenetr Study. The Jouran of Hearth and Lung Transplantation. Vol. 25, Number 8, 2006. M. Zackliczynski et al. Letter:Elective conversion from CellCept to Myfortic under Control of Mycorphenolate Acid Concentration in Stable Heart Transplant Recipients. He Jouran of Heart and Lung Transplantation, Vol. 26, No. 3, 2007. Pharmacokinetics and variability of mycophenolic acid form enteric-coated mycophenolate sodium compared with mycophenolate mofetil in de novo heart transplant recipients. Clin Transplant 2997; 21: 18-23 J. Dumortier et al. Conversion from Mycophenolate Mofetil to Enteric-coated Mycophenolate Sodium in Liver Transplant

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Patients Gastrointestinal Disorders: A Pilot Study. Liver Transplantation 12: 1342-1346, 2006 Cantisani G.P.C.Enteric-coated Mycophenolate Sodium Experience in Liver Transplant Patients. Transplantation Proceedings, 38: 932-933, 2006 H.W. Sollinger. Mycophenolate in transplantation. Clin Transplant 2004;18: 485-492 L. Chan et al. Patient- Reported Gastrointestinal Symptom Burden and Health-Related Quality of Life following Conversion from Mycophenolate Mofetil to Enteric-Coated Mycophenolate Sodium. Transplantation Vol 81, No 9 2006 **Profilassi del rigetto acuto nel trapianto di rene in associazione con Tacrolimus** <u>Trapianto di rene</u> J.M. Puig et al. Comparison of Mycofenolate Mofetil (MMF) and enteric-coated mycophenolate sodium (EC-MPS) pharmacokinetic profile in stable renal transplant (RT) patients treated with tacrolimus (FK) without steroids American Journal of Transplantation 7: 349-349; 780 Suppl. 2 May 2007 P. Bolin et al. Improvement in 3-Month Patient Reported Gastrointestinal Symptoms After Conversion From Mycophenolate Mofetil to Enteric-Coated Mycophenolate Sodium in Renal Transplant Patients Transplantation 2007; 84:1443-1451 K. Budde et al. Conversion from Mycophenolate Mofetil to Enteric-Coated Mycophenolate Sodium in Maintenance Renal Transplant Recipients Receiving Tacrolimus: Clinical Pharmaccokinetics, and Pharmacodynamic Outcomes Transplantations 2007:83:417-424 **Profilassi e terapia della GVHD acuta e cronica nel trapianto di cellule staminali emopoietiche di pazienti adulti e pediatrici refrattari alla terapia di I linea con corticosteroidi** Pharmacokinetics of intravenous mycophenolate mofetil after allogeneic blood stem cell transplantation. Jenke A, Renner U, Richter M, Freiberg-Richter J, Platzbecker U, Helwig A, Thiede H-M, Scha¨fer-Eckart K, Ehninger G, Bornha¨user M. Pharmacokinetics of intravenous mycophenolate mofetil after allogeneic blood stem cell transplantation. Clin Transplantation 2001: 15: 176–184.

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Targeting mycophenolate mofetil for graft-versus-host disease prophylaxis after allogeneic blood stem cell transplantation. I Haentzschel, J Freiberg-Richter, U Platzbecker, A Kiani, J Schetelig, T Illmer, G Ehninger, ESchleyer and M Bornha. Bone Marrow Transplantation (2008) 42, 113–120. Use of intravenous mycophenolate mofetil for graft-versus-host disease prophylaxis in an allogeneic hematopoietic stem cell transplant recipient with an allergic reaction to cyclosporine and tacrolimus. CC Dvorak, E Callard and R Agarwal. Bone Marrow Transplantation (2006) 38, 253–254. Mycophenolate mofetil: fully utilizing its benefits for GvHD prophylaxis. Kentaro Minagawa, Motohiro Yamamori,Yoshio Katayama, Toshimitsu Matsui, Int J Hematol (2012) 96:10–25. **Profilassi del rigetto dopo trapianto di polmone nell'adulto nei casi in cui il micofenolato mofetile comporti effetti collaterali gastrointestinali che richiedano diminuzione/sospensione della dose**. Savvidaki E,Papachristou E,Kazakopoulos P, Papasotiriou M, Vardoulaki M, Goumenos DS. Gastrointestinal disorders after renal transplantation. Transplant Proc. 2014; 46:3183-6. Bunnapradist S, Sampaio MS, Wilkinson AH, Pham PT, Huang E, Kuo HT, Anastasi B, Danovitch GM, Lo SK. Changes in the small bowel of symptomatic kidney transplant recipients converted from mycophenolate Mofetil to enteric---coated mycophenolate sodium. Am J Nephrol. 2014; 40:184-90. Qin Y, Zhang F, Shen B, Liu Y, Qiu J, Guo Y, Fan Y. Efficacy and safety of enteric---coated mycophenolate sodium in patients with de novo and maintenance renal transplantation. Int J Clin Pract Suppl. 2014; 181:17-22 Belliere J, Esposito L, Gandia P, Duffas JP, Sallusto F, Cardeau---Desangles I, Del Bello A, Rostaing L, Kamar N. Comparison of the exposure of mycophenolate mofetil and enteric---coated mycophenolate sodium in recipients of kidney---pancreas transplantation. Ann Transplant. 2014;19:76-81. Sterneck M, Settmacher U, Ganten T, Sarrazin C, Speidel N, Broering D, Heyne N, Paulus E, Mertens M, Fischer L. Improvement in gastrointestinal And health---related quality of life outcomes after conversion from mycophenolate mofetil to enteric---coated mycophenolate sodium In liver transplant recipients. Transplant Proc. 2014; 46:234-40. Ortega F, Sanchez---Fructuoso A, Cruzado JM, Gomez-Alamillo JC, Alarcón A, Pallardó L, Morales JM, Oliver J, Guinea G;

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	MYVIDA Study Group. Gastrointestinal quality of life improvement of renal transplant recipients Converted from mycophenolate mofetil to enteric---coated mycophenolate sodium drugs or agents: mycophenolate mofetil and enteric-coated mycophenolate sodium. Transplantation. 2011; 92:426-32. Toledo AH, Hendrix L, Buchholz V, Fisher E, Newton K, Smith C, Gerber DA. Improvement of gastrointestinal symptoms after conversion from Mycophenolate mofetil to enteric---coated mycophenolate sodium In liver transplant patients. Clin Transplant. 2012;26:156-63. Langone AJ(1), Chan L, Bolin P, Cooper M. Enteric-coated mycophenolate Sodium versus mycophenolate mofetil in renal transplant recipients experiencing gastrointestinal intolerance: a multicenter, double-blind, randomized study. Transplantation 2011; 91:470-8. Lee PH, Vathsala A, Han DJ, Chan TM, Wong HS, Woodcock C, Kurstjens N; Asia Pacific MyPROMS Study Investigators. Conversion to enteric-coated Mycophenolate sodium from mycophenolate mofetil in stable renal transplant patients: results of an Asia-Pacific study. Nephrology (Carlton) 2013;18:57-62. Reinke P, Budde K, Hugo C, Petersen P, Schnuelle P, Fricke L, Scholz D, Sperschneider H, Bahner U, Kramer S, Fischer W, Arns W. Reduction of gastrointestinal complications in renal graft recipients after conversion from mycophenolate mofetil to enteric-coated mycophenolate sodium. Transplant Proc. 2011;43:1641-6. Burg M, Säemann MD, Wieser C, Kramer S, Fischer W, Lhotta K. Enteric-coated mycophenolate sodium reduces gastrointestinal symptoms In renal transplant patients. Transplant Proc. 2009;41:4159-64.
Rapamicina (sirolimus)	**Trapianto fegato; trapianto pediatrico di fegato e/o rene** **Profilassi e terapia trapianto di cellule staminali emopoietiche** **Trapianto pancreas, cuore, polmone** **Trapianto isole di Langerhans** <u>Trapianto di fegato</u> Wiesner R, Klintmalm GB, McDiarmid S, and the Rapamune Liver Transplant Study Group. SIROLIMUS IMMUNOTHERAPY RESULTS IN REDUCED RATES OF ACUTE REJECTION IN DE NOVO ORTHOTOPIC LIVER TRANSPLANT RECIPIENTS. In: American Journal of Transplantation; 2002; Washington; 2002. Maheshwari A, Torbenson MS, Thuluvath PJ. Sirolimus Monotherapy Versus Sirolimus in Combination with Steroidsand/or MMF for Immunosuppression After Liver transplantation. Dig Dis Sci 2006.

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Zaghla H, Selby RR, Chan LS, Kahn JA, Donovan JA, Jabbour N, et al. A comparison of sirolimus vs. calcineurin inhibitor-based immunosuppressive therapies in liver transplantation. Alimentary Pharmacology and Therapeutics 2006;23(4):513-520. Trotter JF, Wallack A, Steinberg T. Low incidence of cytomegalovirus disease in liver transplant recipients receiving sirolimus primary immunosuppression with 3-day corticosteroid taper. Transplant Infect Dis 2003;5(4):174-180. Trotter JF. Sirolimus in liver transplantation. Transplant Proc 2003;35(3 Suppl):S193-200. Neff GW, Montalbano M, Tzakis AG. Ten years of sirolimus therapy in orthotopic liver transplant recipients. Transplant Proc 2003;35(3 Suppl):S209-16. McAlister VC, Peltekian K, Gao Z, Mahalati K, Dominquez J, MacDonald AS. Liver and kidney pancreas transplantation using tacrolimus, sirolimus and steroid immunosuppression. Transplantation 1999;67(9):S601. Watson CJ, Friend PJ, Jamieson NV, Frick TW, Alexander G, Gimson AE, et al. Sirolimus: a potent new immunosuppressant for liver transplantation. Transplantation 1999;67(4):505-509. Kneteman NM, Oberholzer J, Al Saghier M, Meeberg GA, Blitz M, Ma MM, et al. Sirolimus-based immunosuppression for liver transplantation in the presence of extended criteria for hepatocellular carcinoma. Liver Transpl 2004;10(10):1301. Neff GW, Montalbano M, Slapak-Green G, Meyer D, Berney T, Safdar K, et al. Sirolimus therapy in orthotopic liver transplant recipients with calcineurin inhibitor related chronic renal insufficiency. Transplant Proc 2003;35(8):3029-3031. Nair S, Eason J, Loss G. Sirolimus monotherapy in nephrotoxicity due to calcineurin inhibitors in liver transplant recipients. Liver Transpl 2003;9(2):126-9. Nour B, Egidi MF, Cowan PA, Sebastian A, Shokouh-Amiri MH, Vera SH, et al. Safety and effectiveness of conversion to sirolimus in liver transplant recipients with renal dysfunction. in: American Journal of Transplantation; 2002; 2002. Sanchez EQ, Martin AP, Ikegami T, Uemura T, Narasimhan G, Goldstein RM, et al. Sirolimus conversion after liver transplantation: improvement in measured glomerular filtration rate after 2 years. Transplant Proc 2005;37(10):4416-23. Sindhi R, Seward J, Mazariegos G, Soltys K, Seward L, Smith A, et al. Replacing calcineurin inhibitors with mTOR inhibitors in

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	children. Pediatric Transplantation 2005;9(3):391-397. Vester U, Kranz B, Nadalin S, Paul A, Becker J, Hoyer PF. Sirolimus rescue of renal failure in children after combined liver-kidney transplantation. Pediatric Nephrology 2005;20(5):686-9. Casas-Melley AT, Falkenstein KP, Flynn LM, Ziegler VL, Dunn SP. Improvement in renal function and rejection control in pediatric liver transplant recipients with the introduction of sirolimus. Pediatr Transplant 2004;8(4):362-6 <u>Trapianti pediatrici di rene e fegato</u> Sindhi R, Seward J, Mazariegos G, Soltys K, Seward L, Smith A, et al. Replacing calcineurin inhibitors with mTOR inhibitors in children. Pediatric Transplantation 2005;9(3):391-397. Vester U, Kranz B, Nadalin S, Paul A, Becker J, Hoyer PF. Sirolimus rescue of renal failure in children after combined liver-kidney transplantation. Pediatric Nephrology 2005;20(5):686-9. Casas-Melley AT, Falkenstein KP, Flynn LM, Ziegler VL, Dunn SP. Improvement in renal function and rejection control in pediatric liver transplant recipients with the introduction of sirolimus. Pediatr Transplant 2004;8(4):362-6 Markiewicz M, Kalicinski P, Teisseyre J, Ismail H, Kaminski A, Teisseyre M. Rapamycin in children after liver transplantation. Transplant Proc 2003;35(6):2284-6. <u>Trapianti di midollo</u> (GVHD-Stem cell transplantation-malignancy-pediatric).Cutler C, Antin JH. Sirolimus for GVHD prophylaxis in allogeneic stem cell transplantation. Bone Marrow Transplant 2004;34(6):471-6.Rapamycin (sirolimus) for treatment of chronic graft-versus-host disease. Biol Blood Marrow Transplant. 2005; 11: 1: 47-55. Marty FM, Lowry CM, Cutler CS, Campbell BJ, Fiumara K, Baden LR, et al. Voriconazole and Sirolimus Coadministration after Allogeneic Hematopoietic Stem Cell Transplantation. Biol Blood Marrow Transplant 2006;12(5):552-559. <u>Trapianto di pancreas, cuore, polmone</u> Toso C, Baertschiger R, Morel P, Bosco D, Armanet M, Wojtusciszyn A, et al. Sequential kidney/islet transplantation: efficacy and safety assessment of a steroid-free immunosuppression protocol. Am J Transplant 2006;6(5):1049-58. Knight RJ, Kerman RH, Zela S, Podbielski J, Podder H, Van Buren CT, et al. Pancreas transplantation utilizing thymoglobulin, sirolimus, and cyclosporine. Transplantation 2006;81(8):1101-5.

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Gleissner CA, Doesch A, Ehlermann P, Koch A, Sack FU, Katus HA, et al. Cyclosporine Withdrawal Improves Renal Function in Heart Transplant Patients on Reduced-Dose Cyclosporine Therapy. Am J Transplant 2006. Vazquez de Prada JA, Vilchez FG, Cobo M, Ruisanchez C, Valls MF, Ruano J, et al. Sirolimus in de novo heart transplant recipients with severe renal impairment. Transplant International 2006;19(3):245-248. Bestetti R, Theodoropoulos TA, Burdmann EA, Filho MA, Cordeiro JA, Villafanha D. Switch from Calcineurin Inhibitors to Sirolimus-Induced Renal Recovery in Heart Transplant Recipients in the Midterm Follow-up. Transplantation 2006;81(5):692-696. Laporta Hernandez R, Ussetti Gil P, Garcia Gallo C, de Pablo Gafas A, Carreno Hernandez MC, Ferreiro Alvarez MJ. Rapamycin in Lung Transplantation. Transplant Proc 2005;37(9):3999-4000. Sanchez EQ, Martin AP, Ikegami T, Uemura T, Narasimhan G, Goldstein RM, et al. Sirolimus conversion after liver transplantation: improvement in measured glomerular filtration rate after 2 years. Transplant Proc 2005;37(10):4416-23. <u>Trapianto di isole di Langerhans</u> Shapiro AMJ, Lakey JRT, Ryan EA, Korbutt GS, Toth EL, Warnock GL, Kneteman NM, Rajotte RV: Islet transplantation in seven patients with type 1 diabetes mellitus using a glucocorticoid-free immunosuppressive regimen. *N Engl J Med* ; 343:230-238. Shapiro AMJ, Ricordi C, Hering BJ et al: International trial of the Edmonton Protocol for islet transplantation. *N Engl J Med* 2006; 355: 1318-30. Froud T, Baidal DA, Ponte G, Ferreira DV, Ricordi C, Alejandro R: Resolution of neurotoxicity and beta-cell toxicity in an islet transplant recipient following substitution of tacrolimus with MMF. Cell transplant 2006, 15 (7): 613-629 **Terapia immunodepressiva e antirigetto in pazienti adulti e pediatrici sottoposti a tx di intestino e multi-viscerale**. Twenty-five consecutive isolated intestina ltransplants in adult patients: a five-yr clinical experience, Lauro A, Zanfi C, Ercolani G, Dazzi A, Golfieri L, Amaduzzi A, Grazi GL, Vivarelli M, Cescon M, Varotti G, Del Gaudio M, Ravaioli M, Pironi L, Pinna AD. , Clin Transplant 2007: 21: 177–185.

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Influence of Immunosuppression on Alloresponse, Inflammation and Contractile Function of Graft After Intestinal Transplantation, J. Fujishiroa,b,c, T. C. Pecha, T. F. Fingera, M. Praktinjoa, B. Stoffelsa, J. Standopa, K. Abu-Elmagdd, A. Tuerlera, A. Hirnera, J. C. Kalffa and N. Schaefera, American Journal of Transplantation 2010; 10: 1545–1555 Intestinal Transplantation, Loris Pironi, M.D., Michael Staun, M.D., Ph.D., André Van Gossum, M.D., The New England Journal of Medicine 361;24, december 10, 2009: 2388-2389 Intestinal Transplantation, Thomas M. Fishbein, M.D., The New England Journal of Medicine 2009;361: 998-1008 100 Multivisceral Transplants at a Single Center, Andreas G. Tzakis, MD, PhD,* Tomoaki Kato, MD,* David M. Levi, MD,* Werviston DeFaria, MD,*Gennaro Selvaggi, MD,* Debbie Weppler, MSN,* Seigo Nishida, MD, PhD,* Jang Moon, MD,*Juan R. Madariaga, MD, PhD,* Andre I. David, MD,* Jeffrey J. Gaynor, PhD,*John Thompson, MD,† Erick Hernandez, MD,† Enrique Martinez, MD, G. Patricia Cantwell, MD,†Jeffrey S. Augenstein, MD,§ Anthony Gyamfi, MD,§ Ernesto A. Pretto, MD,§ Lorraine Dowdy, MD,‡ Panagiotis Tryphonopoulos, MD,* and Phillip Ruiz, MD, PhD, Annals Surgey 2005; 242: 480–493 The current status of multivisceral transplantation, Qi Mao, You-Sheng Li and Jie-Shou Li, Hepatobiliary Pancreat Dis Int, Vol 8, No 4 • August 15, 2009; 345-350.
Rituximab originatore o biosimilare	**Nei regimi di condizionamento al trapianto di cellule staminali emopoietiche allogeniche in pazienti affetti da patologie ematologiche mediate da cellule CD20 per la profilassi della GVHD cronica in combinazione con fludarabina e ciclofosfoesamide oppure fludarabina e bendamustina.** Solomon SR et al. Safety and efficacy of rituximab-based first line treatment of chronic GVHD. Bone Marrow Transplant. 2019;54(8):1218-1226. Epperla N et al. Fludarabine and Busulfan versus Fludarabine,Cyclophosphamide, and Rituximab as Reduced-Intensity Conditioning for Allogeneic Transplantation in Follicular Lymphoma. Biol Blood Marrow Transplant. 2018; 24(1):78-85. McManigle W, Youssef A, Sarantopoulos S.B cells in chronic graft-versus-host disease. Hum Immunol. 2019; 80(6):393-399. Law AD et al. Reduced-Intensity Conditioning and Dual T Lymphocyte Suppression with Antithymocyte Globulin and Post-Transplant Cyclophosphamide as Graft-versus-Host Disease Prophylaxis in Haploidentical Hematopoietic Stem Cell Transplants for Hematological Malignancies. Biol Blood Marrow Transplant. 2018; 24(11):2259-2264.

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Khouri IF et al. BFR (bendamustine, fludarabine, and rituximab) allogeneic conditioning for chronic lymphocytic leukemia/lymphoma: reduced myelosuppression and GVHD. Blood. 2014 Oct 2;124(14):2306-12. Rituximab prophylaxis prevents corticosteroid-requiring chronic GVHD after allogeneic peripheral blood stem cell transplantation: results of a phase 2 trial. Cutler C, Kim HT, Bindra B, Sarantopoulos S, Ho VT, Chen YB, Rosenblatt J, McDonough S, Watanaboonyongcharoen P, Armand P, Koreth J, Glotzbecker B, Alyea E, Blazar BR, Soiffer RJ, Ritz J, Antin JH. Blood. 2013 Aug 22;122(8):1510-7. Prophylactic rituximab after allogeneic transplantation decreases B-cell alloimmunity with low chronic GVHD incidence. Arai S, Sahaf B, Narasimhan B, Chen GL, Jones CD, Lowsky R, Shizuru JA, Johnston LJ, Laport GG, Weng WK, Benjamin JE, Schaenman J, Brown J, Ramirez J, Zehnder JL, Negrin RS, Miklos DB.Blood. 2012 Jun 21;119(25):6145-54. Rituximab reduces the incidence of acute graft-versus-host disease. Christopeit M, Schütte V, Theurich S, Weber T, Grothe W, Behre G. Blood. 2009 Mar 26;113(13):3130-1. Rituximab for steroid-refractory chronic graft-versus-host disease. Corey Cutler, David Miklos, Haesook T. Kim, Nathaniel Treister, Sook-Bin Woo, Don Bienfang, Lloyd B. Klickstein, Jesse Levin, Katherine Miller, Carol Reynolds, Rebecca Macdonell, Mildred Pasek, Stephanie J. Lee, Vincent Ho, Robert Soiffer, Joseph H. Antin, Jerome Ritz, and Edwin Alyea. Blood, 2006 15 July; 108 (2):756 – 762.
Siero antilinfocitario di cavallo	**Regime di condizionamento nel trapianto autologo per malattie autoimmuni** High-dose immunosuppressive therapy and autologous peripheral blood stem cell transplantation for severe multiple sclerosis.Nash RA, Bowen JD, McSweeney PA, Pavletic SZ, Maravilla KR, Park MS, Storek J, Sullivan KM, Al-Omaishi J, Corboy JR, DiPersio J, Georges GE, Gooley TA, Holmberg LA, LeMaistre CF, Ryan K, Openshaw H, Sunderhaus J, Storb R, Zunt J, Kraft GH.Blood. 2003 Oct 1;102(7):2364-72. Brazilian experience with two conditioning regimens in patients with multiple sclerosis: BEAM/horse ATG and CY/rabbit ATG Hamerschlak N, Rodrigues M, Moraes DA, Oliveira MC, Stracieri AB, Pieroni F, Barros GM, Madeira MI, Simões BP, Barreira AA, Brum DG, Ribeiro AA, Kutner JM, Tylberi CP, Porto PP, Santana CL, Neto JZ, Barros JC, Paes AT, Burt RK, Oliveira EA, Mastropietro AP, Santos AC, Voltarelli JC. Bone Marrow Transplant. 2010 Feb;45(2):239-48

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
Tacrolimus	**Profilassi AR in trapianto di cuore-polmone, trapianto polmone, trapianto pancreas, trapianto rene - pancreas, trapianto intestino, trapianto isole di Langerhans.** **Profilassi AR e trattamento e profilassi GVHD acuta e cronica in trapianto di cellule staminali emopoietiche nell'adulto e nel bambino** Profilassi Tx polmone: - Treede et Al, 3rd ICI San Diego, US, 2004; abstract 22 - Keenan et Al, Ann Thoracic Surg 1995,60:580 - Treede et Al, J Heart Lung Transplant 2001; 20:511 Profilassi Tx Rene pancreas e pancreas: - Bechstein et Al, Transplantation 2004;7:1221 - J Malaise et Al and EUROSPK Study Group, Tranpslantation Proceedings 2005 37,2843-2845 - F Saudek and the SPK Study Group, Nephrology Dialysis Transplantation 2005 Profilassi Tx Intestino-Multiviscerale: Abu Elmagd et Al, Ann Surg 2001;234:404 Trapianto di Midollo: - Koehler MT et Al Bone Marrow Transplantation 1995 15:895 - Kananaru A et Al for the Japanese FK 506 Study Group; Bone Marrow Transplantation 1995 15:885 - Nash R.A et Al Blood 1995 85: 3746 - Nash R.A et Al Blood 1996 88:3634 - Nash R.A et Al Blood 2000 96:2062-2068 Trapianto di isole di Langerhans Shapiro AMJ, Lakey JRT, Ryan EA, Korbutt GS, Toth EL, Warnock GL, Kneteman NM, Rajotte RV: Islet transplantation in seven patients with type 1 diabetes mellitus using a glucocorticoid-free immunosuppressive regimen. *N Engl J Med* ; 343:230-238

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Shapiro AMJ, Ricordi C, Hering BJ et al: International trial of the Edmonton Protocol for islet transplantation. *N Engl J Med* 2006; 355: 1318-30, **Tutte le indicazioni anche in associazione con altri farmaci ad attività immunosoppressiva o immunomodulante e/o steroide**. Bibliografia associazioni: Generale: Undre N., Nephrol Dial Transplant (2003) 18 [Suppl 1]: i12–i15; Andreoni KA et al., American Journal of Transplantation 2007; 7 (Part 2): 1359–1375; Guerra G. et al., Transplant International ISSN 0934-0874; Webster A. et al., BMJ, doi:10.1136/bmj.38569.471007 Micofenolato Mofetile (MMF):Vitko S. et al. ,Transplantation 2005;80: 1734–1741; Squifflet JP et al., Transplantation Proceedings, 34, 1584–1586 (2002); Rostaing L. et al., Transplantation • Volume 79, Number 7, April 15, 2005; Mc Taggart S., NEPHROLOGY 2007; 12, S106–S110; Augustine j.j. et al., Transplantation 2006;81: 1004–1009; H.T. Silva et al., American Journal of Transplantation 2007; 7: 595–608; Ekberg H. et al., N Engl J Med 2007;357:2562-75; McAlister H. et al., Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD005161. DOI: 10.1002/14651858.CD005161.pub2; Pageaux GP. Et al., LIVER TRANSPLANTATION 12:1755-1760, 2006; Grimm M. et al., American Journal of Transplantation 2006; 6: 1387–1397; Kobashigawa JA et al., American Journal of Transplantation 2006; 6: 1377–1386; Bravo C. et al., Transplantation Proceedings, 39, 2409–2412 (2007); Gallon LG et al., Transplantation 2007;83: 1324–1329 Acido Micofenolico: Budde K. Et al., Transplantation 2007;83: 417–424 Sirolimus: Vitko S. et al. ,Transplantation 2005;80: 1734–1741; ; Augustine j.j. et al., Transplantation 2006;81: 1004–1009; ; Kobashigawa JA et al., American Journal of Transplantation 2006; 6: 1377–1386; Ciancio G. et al., Transplantation 2006;81: 845–852 Everolimus: Chan L. et al., Transplantation 2008;85: 821–826; Kovarik JM et al., Transplantation Proceedings, 38, 3456–3458 (2006) Azatioprina: Grimm M. et al., American Journal of Transplantation 2006; 6: 1387–1397; Bravo C. et al., Transplantation Proceedings, 39, 2409–2412 (2007); Jessupp M et al., Curr. Opin.in organ Transplantation 12: 536-542 (2007)

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Anticorpi (mono o policlonali): Boillot O. et al., Liver Transplantation, Vol 11, No 1 (January), 2005: pp 61–67; H.T. Silva et al., American Journal of Transplantation 2007; 7: 595–608; Kobashigawa JA et al., American Journal of Transplantation 2006; 6: 1377–1386; Rostaing L. et al., Transplantation • Volume 79, Number 7, April 15, 2005; Bravo C. et al., Transplantation Proceedings, 39, 2409–2412 (2007); Maudgil A et al., Pediatr. Drugs 2007 9(5)
Treosulfano	**Nei regimi di condizionamento del trapianto di cellule staminali emopoietiche (CSE) del bambino e dell'adulto affetti da patologia oncologica e non oncologica ad alto rischio di tossicità.** Bitan M, Shapira MY, et al., Exp Hematol. 2005 Jun; Casper J, Freund M. Int J Clin Pharmacol Ther. 2004;42(11):661-2. Hilger RA, Baumgart J, et al.,Int J Clin Pharmacol Ther. 2004;42(11):654-5. Beelen DW, Trenschel R, et al.,Bone Marrow Transplant. 2005 Feb; Shimoni A, Kröger N, et al.,Leukemia. 2005 Jan; Casper J, Knauf W, Blau I, et al.,Ann Hematol. 2004; Casper J, Knauf W, Kiefer T, et al.,Blood. 2004 Jan 15; Bacher U, Klyuchnikov E, et al.,.Expert Opin Drug Saf. 2009 May; Cutting R, Mirelman A, Vora A.Br J Haematol. 2008 Dec; Główka FK, Karaźniewicz-Łada M, et al.,Bone Marrow Transplant. 2008 Oct; Bernardo ME, Zecca M, et al.,Br J Haematol. 2008 Nov; Baronciani D, Rambaldi A, et al., Am J Hematol. 2008 Sep;

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Holowiecki J, Giebel S, et al.,. Br J Haematol. 2008 Jun; Shimoni A, Hardan I, et al.,Leuk Lymphoma. 2007 Dec; Giebel S, Wojnar J, et al., Ann Transplant. 2006; Blau IW, Schmidt-Hieber M, et al., Ann Hematol. 2007 Aug; Schmidt-Hieber M, Blau IW, et al.,Bone Marrow Transplant. 2007 Apr; Sauer M, Zeidler C, et al.,Bone Marrow Transplant. 2007 Feb; Kröger N, Shimoni A, et al.,Bone Marrow Transplant. 2006 Feb; Casper J, Wilhelm S, et al.,Dtsch Med Wochenschr. 2005 Sep 23; Wandt H, Schaefer-Eckart K, et al.,Haematologica. 2005 Sep;
Valganciclovir	**Trapianto di cellule staminali emopoietiche; trapianto d'organo solido in pazienti adulti e pediatrici**. <u>BMT</u> Winston DJ et al. Pharmacokinetics of ganciclovir after oral valganciclovir versus intravenous ganciclovir in allogeneic stem cell transplant patients with graft-versus-host disease of the gastrointestinal tract. Biol Blood Marrow Transplant 2006; 12 (6): 635-40 The pharmacokinetics of ganciclovir after oral valganciclovir versus intravenous ganciclovir were compared in allogeneic stem cell transplant recipients with stable graft-versus-host disease of the gastrointestinal tract. Oral valganciclovir could be a useful alternative to intravenous ganciclovir in certain stable stem cell transplant patients who require prophylaxis or preemptive therapy for cytomegalovirus infection. Ayala E et al. Valganciclovir is safe and effective as pre-emptive therapy for CMV infection in allogeneic hematopoietic stem cell transplantation. Bone Marrow Transplant 2006; 37 (9): 851-6 Pre-emptive therapy of CMV infection with oral VGC is safe and effective in allogeneic HSCT recipients. Van der Heiden PLJ et al. Oral valganciclovir as pre-emptive therapy has similar efficacy on cytomegalovirus DNA load reduction as intravenous ganciclovir in allogeneic stem cell transplantation recipients. Bone Marrow Transplant 2006; 37 (7): 693-8

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	The efficacy and safety of oral valganciclovir was compared to ganciclovir i.v. in pre-emptive treatment of cytomegalovirus (CMV) in T-cell-depleted allogeneic stem cell transplant (allo-SCT) recipients. In conclusion, pre-emptive treatment with valganciclovir and ganciclovir, led to similar reduction of CMV DNA load. Oral valganciclovir is an attractive and safe alternative for pre-emptive CMV treatment in T-cell-depleted allo-SCT recipients. Einsele H et al. Oral valganciclovir leads to higher exposure to ganciclovir than intravenous ganciclovir in patients following allogeneic stem cell transplantation. Blood 2006; 107 (7): 3002-8 This supports the use of V-GCV in SCT, even in patients with I-GVHD grades I-II. Due to higher exposure after V-GCV compared with IV-GCV, patients should be monitored carefully for safety reasons. Boeckh M et al. Cytomegalovirus in hematopoietic stem cell transplant recipients: Current status, known challenges, and future strategies. Biol Blood Marrow Transplant 2003; 9 (9): 543-58 Strategies currently being investigated include long-term suppression of CMV with valganciclovir for the prevention of late CMV infection and disease, adoptive transfer of CMV-specific T cells, and donor and recipient vaccination strategies. <u>Infezione da Cytomegalovirus in pazienti pediatrici con trapianto</u> Clark BS et al. Valganciclovir for the prophylaxis of cytomegalovirus disease in pediatric liver transplant recipients. Transplantation. 2004; 77 (9): 1480 Burri M et al. Oral valganciclovir in children: single dose pharmacokinetics in a six-year-old girl. Ped Infectious Dis J 2004; 23 (3): 263-266 Razonable RR, Paya CV. Valganciclovir for the prevention and treatment of cytomegalovirus disease in immunocompromised hosts. Expert Rev. Anti-infect. Ther. 2004; 2 (1): 27–42) Vaudry W et al. Safeto of oral valganciclovir powder for oral solution in pediatric solid organ transplant recipients. Am J Transplant / Transplantation 2006 WTC 215 Abs 441. Bouw R et al. Ganciclovir pharmacokinetics in pediatric solid organ transplant recipients after administration of valganciclovir oral solution. Am J Transplant / Transplantation 2006 WTC 215 Abs 442. **E’ ammesso l’utilizzo del valganciclovir come terapia preventiva della malattia da CMV nei pazienti sottoposti a trapianto di rene.**

Principio attivo	Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura
	Kalpoe JS et al. Similar reduction of cytomegalovirus DNA load by oral valganciclovir and intravenous ganciclovir on pre-emptive therapy after renal and renal-pancreas transplantation. Antivir Ther (Lond). 2005. Khoury JA et al. Prophylactic Versus Preemptive Oral Valganciclovir for the Management of Cytomegalovirus Infection in Adult Renal Transplant Recipients. Am J Transplant. 2006 Lopau K et al. Efficacy and safety of preemptive anti-CMV therapy with valganciclovir after kidney transplantation. Clin Transplant. 2007. Said T et al. Oral Valgancyclovir Versus Intravenous for Cytomegalovirus Prophylaxis in Kidney Transplant Recipient. Transplantation Proceedings. 2007 Reischig T et al. Intragraft cytomegalovirus infection: a randomized trial of valacyclovir prophylaxis versus pre-emptive therapy in renal transplant recipients. Antivir Ther (Lond). 2010 **E' ammesso l'utilizzo del valganciclovir come terapia preventiva della malattia da CMV nei pazienti sottoposti a trapianto di organo solido.** Diaz-Pedroche C et al. Efficacy and Safety of Valgancyclovir as Preemptive Therapy for the Prevention of Cytomegalovirus Disease in Solid Organ Transplant Recipients. Transplantation Proceedings 2005 Strippoli GF et al. Pre-emptive treatment for cytomegalovirus viraemia to prevent cytomegalovirus disease in solid organ transplant recipients. Cochrane Database Syst Rev. 2006 Asberg A et al. Oral valganciclovir is an effective and safe treatment option for CMV disease in solid organ transplant recipients Am J Transplant. 2007 Sun H-Y et al. Prevention of Posttransplant Cytomegalovirus Disease and Related Outcomes with Valganciclovir: A Systematic Review. Am J Transplant. 2008. **Trapianto di cellule staminali emopoietiche allogeniche in pazienti pediatrici** Prophylaxis against cytomegalovirus infection in pediatric and adult patients undergoing solid organ and hematopoietic stem cells transplantation. Ferrés M, Nervi B, Ramírez P. Rev Chilena Infectol. 2012 Sep;29 Suppl 1:S23-8