ALLEGATO 5

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

Nome composto	Indicazioni già autorizzate	**Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura.**
Basiliximab	Indicato per la profilassi del rigetto acuto in pazienti adulti e pediatrici sottoposti a trapianto renale allogenico *de novo*. Deve essere usato in associazione ad un trattamento immunosoppressivo a base di ciclosporina in microemulsione e corticosteroidi nei pazienti con una quantità di anticorpi reattivi inferiore all'80%, o in uno schema terapeutico immunosoppressivo di mantenimento in triplice terapia comprendente ciclosporina in microemulsione, corticosteroidi e azatioprina o micofenolato mofetile.	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 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-

Nome composto	Indicazioni già autorizzate	**Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura.**
		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) **Trapianto di isole di Langerhans** 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 **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.
Everolimus	Profilassi del rigetto d'organo in pazienti adulti, a rischio immunologico da lieve a moderato, sottoposti a trapianto renale o cardiaco allogenico. Certican deve essere utilizzato in associazione con ciclosporina in microemulsione e corticosteroidi.	Profilassi del rigetto acuto in pazienti pediatrici sottoposti a trapianto di rene. Profilassi del rigetto acuto in pazienti adulti sottoposti a trapianto di polmone. Profilassi del rigetto acuto in pazienti adulti sottoposti a trapianto di fegato. 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

Nome composto	Indicazioni già autorizzate	**Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura.**
		renal transplant patients. Pediatric Transplantation 2002; 6: 147-152 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
Immunoglobulina di coniglio antitimocitaria	Profilassi nell'adulto della malattia acuta e cronica da trapianto verso ospite in trapianti da donatore familiare non immunocompatibile o immunocompatibile non familiare (Graft versus Host Disease, GvHD)	Trattamento nell'adulto della malattia acuta e cronica da trapianto verso ospite (Graft versus Host Disease, GvHD) Profilassi e trattamento nel paziente pediatrico della malattia acuta e cronica da trapianto verso ospite (Graft versus Host Disease, GvHD) 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 disorders and CML B Horn, L-A Baxter-Lowe, L Englert, A McMillan, M Quinn, K DeSantes and M Cowan

Nome composto	Indicazioni già autorizzate	**Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura.**
		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
Micofenolato Mofetile	Trapianto rene; trapianto rene pediatrico; trapianto cuore; trapianto fegato	Trapianto cuore pediatrico; trapianto fegato pediatrico; trapianto pancreas; trapianto polmone; trapianto di midollo osseo; trapianto isole di Langerhans **Trapianto di cuore pediatrico** 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 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 **Trapianto di Fegato pediatrico** 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.*

Nome composto	Indicazioni già autorizzate	**Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura.**
		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): 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 **Trapianto di Pancreas** 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 *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*

Nome composto	Indicazioni già autorizzate	**Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura.**
		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 **Trapianto di Polmone** 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; 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.* Trapianto di isole di Langerhans

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		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
Micofenolato Sodico	Myfortic è indicato in associazione con ciclosporina e corticosteroidi, per la profilassi del rigetto acuto, in pazienti adulti che ricevono un trapianto allogenico di rene.	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 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
Rapamicina	Trapianto rene	Trapianto fegato; trapianto pediatrico di fegato e/o rene; trapianto midollo;trapianto pancreas, cuore, polmone. Trapianto isole di Langerhans **Trapianto di fegato** 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. 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.

Nome composto	Indicazioni già autorizzate	**Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura.**
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Nome composto	Indicazioni già autorizzate	**Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura.**
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Tacrolimus	Profilassi AR e trattamento AR in: trapianto rene, trapianto fegato, trapianto cuore; trattamento AR in: trapianto rene-pancreas, trapianto pancreas, trapianto cuore-polmone, trapianto polmone, trapianto intestino multiviscerale	Profilassi AR in trapianto di cuore-polmone, trapianto polmone, trapianto pancreas, trapianto rene - pancreas, trapianto intestino trapianto isole di Langerhans; profilassi AR e trattamento GVHD in trapianto midollo osseo **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**:

Nome composto	Indicazioni già autorizzate	**Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura.**
		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 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,
Valganciclovir	Prevenzione della malattia da CMV in pazienti CMV negativi e sottoposti a trapianto d'organo SOLIDO da donatore CMV positivo. trattamento di induzione e mantenimento della retinite da CMV in pazienti con AIDS.	Trapianto midollo osseo; trapianto d'organo solido pediatrico **BMT** 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 *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.*

Nome composto	Indicazioni già autorizzate	**Estensione di indicazione relative ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura.**
		Infezione da Cytomegalovirus in pazienti pediatrici con trapianto 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.