

FARMACI CON EVIDENZA SCIENTIFICA A SUPPORTO DELL'USO IN PEDIATRIA
PER INDICAZIONI TERAPEUTICHE DIVERSE DA QUELLE AUTORIZZATE

ATC = J (Antiinfettivi)

Principio attivo	Indicazione terapeutica off-label	Referenze di letteratura
MINOCICLINA	Trattamento dell'acne Brucellosi Profilassi antibiotica in pazienti con CVC a lunga permanenza Rickettsiosi	- Ozolins M, et al. Randomised controlled multiple treatment comparison to provide a cost-effectiveness rationale for the selection of antimicrobial therapy in acne. <i>Health Technol Assess.</i> 2005 Jan;9(1):iii-212.
		- Fleischer AB Jr, et al. Safety and efficacy of a new extended-release formulation of minocycline. <i>Cutis.</i> 2006 Oct;78(4 Suppl):21-31.
		- Stewart DM, et al. Dose-ranging efficacy of new once-daily extended-release minocycline for acne vulgaris. <i>Cutis.</i> 2006 Oct;78(4 Suppl):11-20.
		- Ozolins M, et al. Comparison of five antimicrobial regimens for treatment of mild to moderate inflammatory facial acne vulgaris in the community: randomised controlled trial. <i>Lancet.</i> 2004 Dec 18-31;364(9452):2188-95.
		Cascio A, Di Liberto C, D'Angelo M. No findings of dental defects in children treated with minocycline. <i>Antimicrob Agents Chemother.</i> 2004 Jul;48(7):2739-41.
LEVOFLOXACINA	Infezioni gravi da Gram + e Gram - in pazienti immunocompromessi a gestione ospedaliera e TBC	- Hwang DG, Schanzlin DJ, Rotberg MH, Foulks G, Raizman MB; Levofloxacin Bacterial Conjunctivitis Place-controlled Study Group. A phase III, placebo controlled clinical trial of 0.5% levofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis. <i>Br J Ophthalmol.</i> 2003 Aug;87(8).
		- Noel GJ, Blumer JL, Pichichero ME. A randomized comparative study of levofloxacin versus amoxicillin/clavulanate for treatment of infants and young children with recurrent or persistent acute otitis media. <i>Pediatr Infect Dis J.</i> 2008 Jun;27(6):483-9. RCT
		- Bradley JS, Arguedas A, Blumer JL. Comparative study of levofloxacin in the treatment of children with community-acquired pneumonia. <i>Pediatr Infect Dis J.</i> 2007 Oct;26(10):868-78.
		- Lichtenstein SJ, Rinehart M. Efficacy and safety of 0.5% levofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis in pediatric patients. <i>J AAPOS</i> 2003; 7(5): 317-324.
		Chien SC, Welss TG, Blumer JL. Levofloxacin pharmacokinetics in children. <i>J Clin Pharmacol</i> 2005; 45:153-160.
ITRACONAZOLO	Trattamento delle infezioni fungine cutanee (tinea capitis (micosi cutanee)), trattamento delle infezioni micotiche sistemiche inefficaci ad altri antimicotici, candidosi orale e/o esofagea dei pazienti HIV-positivi o di altri pazienti immunocompromessi non rispondenti ad	Mondal RK, et al. Randomized comparison between fluconazole and itraconazole for the treatment of candidemia in a pediatric intensive care unit: a preliminary study. <i>Pediatr Crit Care Med</i> 2004;5:561-65;
		Singhi SC, et al. Oral itraconazole in treatment of candidemia in a pediatric intensive care unit. <i>Indian J Pediatr</i> 2004;71:973-77;
		Groll AH, et al. Safety, pharmacokinetics and pharmacodynamics of cyclodextrin itraconazole in pediatric

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	altre terapie, profilassi infezioni fungine profonde in pazienti con neoplasie ematologiche o sottoposti a BMT a rischio di neutropenia, profilassi aspergillosi in malattia granulomatosa cronica	<p>patients with orofaringeal candidiasis. Antimicrob Agents Chemother 2002;46:2554-63;</p> <p>Schmitt C, et al. Pharmacokinetics of itraconazole oral solution in neutropenic children during long-term prophylaxis. Antimicrob Agents Chemother 2001;45:1561-64;</p> <p>Abdel-Rahman SM, et al. Single-dose pharmacokinetics of intravenous itraconazole and hydroxypropyl-β-ciclodextrin in infants, children, adolescents. Antimicrob Agents Chemother 2007;51:2668-73;</p> <p>De Repentigny L, et al. Repeated-dose pharmacokinetics of an oral solution of itraconazole in infants and children. Antimicrob Agents Chemother 1998;42:404-08;</p> <p>Foot AB, et al. Itraconazole oral solution as antifungal prophylaxis in children undergoing stem cell transplantation or intensive chemotherapy for haematological disorders. Bone Marrow Transplant 1999;24:1089-93.</p>
PIRAZINAMIDE	Trattamento della tubercolosi in associazione con altri farmaci (uso ospedaliero)	<p>- Swaminathan S. et al. Short-course chemotherapy for paediatric respiratory tuberculosis: 5-year report. Int J Tuberc Lung Dis. 2005 Jun;9(6):693-6. RCT</p> <p>- Te Water Naude JM, et al. Twice weekly vs. daily chemotherapy for childhood tuberculosis. Pediatr Infect Dis J. 2000 May;19(5):405-10. RCT</p> <p>- Magdorf K, et al. Compliance and tolerance of new antitubercular short-term chemopreventive regimens in childhood--a pilot project Pneumologie. 1994 Oct;48(10):761-4.</p> <p>- Peter R. Donald and H. Simon Schaaf. MINI-SYMPOSIUM: CHILDHOOD TUBERCULOSIS Old and new drugs for the treatment of tuberculosis in children. PAEDIATRIC RESPIRATORY REVIEWS (2007) 8, 134-141.</p> <p>National Collaborating Centre for Chronic Conditions. Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control. London (UK): Royal College of Physicians; 2006. 215 p.</p> <p>Gupta P, Roy V, Rai Sethi G. Pyrazinamide blood concentrations in children suffering from tuberculosis: a comparative study at two doses. RCT</p>
ETAMBUTOLO	trattamento della tubercolosi in associazione con altri farmaci (uso ospedaliero)	<p>- Chemotherapy and management of tuberculosis in the United Kingdom: recommendations 1998. Joint Tuberculosis Committee of the British Thoracic Society. Thorax. 1998 Jul;53(7):536-48.</p> <p>- Treatment of tuberculosis and tuberculosis infection in adults and children. American Thoracic Society. Monaldi Arch Chest Dis. 1994 Sep;49(4):327-45.</p> <p>- Initial therapy for tuberculosis in the era of multidrug resistance. Recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR Recomm Rep. 1993 May 21;42(RR-7):1-8.</p> <p>- Peter R. Donald and H. Simon Schaaf MINI-SYMPOSIUM: CHILDHOOD TUBERCULOSIS Old and new drugs for the treatment of tuberculosis in children. PAEDIATRIC RESPIRATORY REVIEWS (2007) 8, 134-141.</p> <p>National Collaborating Centre for Chronic Conditions. Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control. London (UK): Royal College of Physicians; 2006. 215 p.</p>

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		<p>- Trebucq. Sholud etambutol be recommendede for routine treatment of tuberculosis in children? A review of literature. Int J Tuberc Lung Dis 1997; 1(1):12-15.</p> <p>Thee S, Detjen A, Quarcoo D. Ethambutol in paediatric tuberculosis: aspect of ethambutol serum concentration, efficacy and toxicity in children. Int J Tuberc Lung Dis 2007;11(9):965-971.</p>
GANCICLOVIR	<p>Profilassi e trattamento delle infezioni da citomegalovirus nei pazienti immunocompromessi.</p> <p>Trattamento delle infezioni congenite e prenatali con dimostrata localizzazione d'organo.</p>	<p>Tezer H et al. Cytomegalovirus hepatitis and ganciclovir treatment in immunocompetent children. Turk J Pediatr 2008; 50 (3): 228-234</p> <p>Spivey JF et al. Safety and efficacy of prolonged cytomegalovirus prophylaxis with intravenous ganciclovir in pediatric and young adult lung transplant recipients. Pediatr Transplant 2007; 11 (3): 312-318</p> <p>Shereck EB et al. A pilot phase II study of alternate day ganciclovir and foscarnet in preventing cytomegalovirus (CMV) infections in at-risk pediatric and adolescent allogenic stem cell transplant recipients. Pediatr Blood Cancer 2007; 49 (3): 306-312</p> <p>Melgosa Hijosa M et al. Preemptive treatment with oral ganciclovir for pediatric renal transplantation. Clin Nephrol 2004; 61 (4): 246-252</p> <p>Hadaya K et al. Ganciclovir for severe cytomegalovirus primary infection in an immunocompetent child. Eur J Clin Microbiol Infect Dis 2004; 23 (3): 218-220</p> <p>Zhang D et al. Pharmacokinetics of ganciclovir in pediatric renal transplant recipients. Pediatr Nephrol 2003; 18 (9): 943-948</p> <p>Avila-Aguero ML, et al. Ganciclovir therapy in cytomegalovirus (CMV) infection in immunocompetent pediatric patients. Int J Infect Dis. 2003 Dec;7(4):278-81.</p> <p>Burns LJ,et al. Randomized clinical trial of ganciclovir vs acyclovir for prevention of cytomegalovirus antigenemia after allogeneic transplantation. Bone Marrow Transplant. 2002 Dec;30(12):945-51.</p> <p>Frenkel LM, et al. Oral ganciclovir in children: pharmacokinetics, safety, tolerance, and antiviral effects. The Pediatric AIDS Clinical Trials Group.</p>
VALGANCICLOVIR	<p>Trattamento delle infezioni da citomegalovirus in pazienti pediatrici con sintomatologia grave riconducibile all'infezione (prevalentemente ipoacusia neurosensoriale), sia come opzione terapeutica ex novo, sia come mantenimento dopo la terapia iniziale endovenosa con il medicinale ganciclovir.</p>	<p>Kimberlin DW et al. Pharmacokinetic and Pharmacodynamic Assessment of Oral Valganciclovir in the treatment of symptomatic congenital cytomegalovirus disease. J Infect Dis. 2008;197(6):836-45.</p> <p>Amir et al. Treatment of symptomatic congenital CMV infection with intravenous ganciclovir followed by long-term oral valganciclovir. Eur J Ped 2010; 169: 1061-67.</p> <p>Kimberlin DW et al. Valganciclovir for symptomatic congenital cytomegalovirus disease. N Engl J Med. 2015; 372(10):933-43.</p> <p>Bilavsky E. et al. Hearing outcome of infants with congenital cytomegalovirus and hearing impairment. Arch Dis Child 2016;101(5):433-8.</p>

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FOSCARNET	OPBG: Trattamento delle infezioni/riattivazioni da CMV in pazienti immunocompromessi resistenti al ganciclovir o nei quali l'utilizzo del ganciclovir sia controindicato. Trattamento dell'infezione da HSV 1/2 e VZV resistente all'acyclovir in pazienti immunocompromessi.	<p>Pediatrici: solo case report</p> <p>Shereck EB et al. A pilot phase II study of alternate day ganciclovir and foscarnet in preventing cytomegalovirus (CMV) infections in at-risk pediatric and adolescent allogenic stem cell transplant recipients. <i>Pediatr Blood Cancer</i> 2007; 49 (3): 306-312</p> <p>Khurana RN et al. Intravenous foscarnet in the management of acyclovir-resistant herpes simplex virus type 2 in acute retinal necrosis in children. <i>Med Sci Monit</i> 2005; 11 (12): CS75-78</p> <p>Ahmed AM et al. Managing herpes zoster in immunocompromised patients. <i>Herpes</i> 2007; 14 (2): 32-36</p> <p>Ohta H, et al. Foscarnet therapy for ganciclovir-resistant cytomegalovirus retinitis after stem cell transplantation: effective monitoring of CMV infection by quantitative analysis of CMV mRNA. <i>Bone Marrow Transplant</i>. 2001 Jun;27(11):1141-5.</p> <p>Sastry SM, et al. Combined ganciclovir and foscarnet in pediatric cytomegalovirus retinitis. <i>J Natl Med Assoc</i>. 1996 Oct;88(10):661-2.</p> <p>Gnann JW Jr, Salvaggio MR. Drugs for herpesvirus infections. In: Cohen J, Powderly WG, Eds: <i>Infectious Diseases</i>. Mosby: London 2004; pp 1895-1909 (spec 1905)</p> <p>Walton RC, et al. Combined intravenous ganciclovir and foscarnet for children with recurrent cytomegalovirus retinitis. <i>Ophthalmology</i>. 1995 Dec;102(12):1865-70.</p>
FLUCITOSINA	infezioni sistemiche da funghi e lieviti (candidosi, meningite criptococcica) non in monoterapia	<p>Chotmongkol V, et al. Comparison of amphotericin B, flucytosine and itraconazole with amphotericin B and flucytosine in the treatment of cryptococcal meningitis in AIDS. <i>J Med Assoc Thai</i>. 1997 Jul;80(7):416-25.</p> <p>- Frattarelli DA, et al. Antifungals in systemic neonatal candidiasis. <i>Drugs</i>. 2004;64(9):949-68.</p> <p>- Bliss JM, et al. Antifungal pharmacotherapy for neonatal candidiasis. <i>Semin Perinatol</i>. 2003 Oct;27(5):365-74.</p>
RIBAVIRINA	Trattamento delle infezioni da VRS nei neonati e nei bambini con fattori di rischio (prematurità, broncodisplasia, cardiopatie congenite, pazienti immunodepressi).	<p>Ventre K, Randolph AG. Ribavirin for respiratory syncytial virus infection of the lower respiratory tract in infants and young children.</p> <p><i>Cochrane Database Syst Rev</i>. 2007 Jan 24; Gluud LL, Krogsgaard K, Gluud C. ribavirin with or without alpha interferon for chronic hepatitis C</p> <p><i>Cochrane Database Syst Rev</i>. 2007 Jul 18; Palumbo E. treatment for chronic hepatitis C in children a review. <i>Am j.ther</i> 2009 feb 28</p>
TENOFIVIR	HIV in età pediatrica nei pazienti plurifalliti (dopo stadio Turner III)	<p>- Viganò A, et al. Improvement in dyslipidaemia after switching stavudine to tenofovir and replacing protease inhibitors with efavirenz in HIV-infected children. <i>Antivir Ther</i>. 2005;10(8):917-24.</p> <p>- Rosso R, Nasi M, Di Biagio A. Effects of the change from Stavudine to tenofovir in human immunodeficiency virus-infected children treated with highly active antiretroviral therapy: studies on mitochondrial toxicity and thymic function. <i>Pediatr Infect Dis J</i>. 2008 Jan;27(1):17-21. RCT</p>

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		<p>- Viganò A, Brambilla P, Cafarelli L. Normalization of fat accrual in lipotrophic, HIV-infected children switched from stavudine to tenofovir and from protease inhibitor to efavirenz. <i>Antivir Ther.</i> 2007;12(3):297-302.</p> <p>- Riordan A, Judd A, Boyd K. Collaborative HIV Paediatric Study. Tenofovir use in human immunodeficiency virus-1-infected children in the United Kingdom and Ireland. <i>Pediatr Infect Dis J.</i> 2009 Mar;28(3):204-9.</p> <p>- Viganò A, Zuccotti GV, Martelli L. Renal safety of tenofovir in HIV-infected children: a prospective, 96-week longitudinal study. <i>Clin Drug Investig.</i> 2007;27(8):573-81.</p> <p>- Giacomet V, Mora S, Martelli L. A 12-month treatment with tenofovir does not impair bone mineral accrual in HIV-infected children. <i>J Acquir Immune Defic Syndr.</i> 2005 Dec 1;40(4):448-50.</p>
CASPOFUNGINA	Aspergillosi invasiva in pazienti refrattari o intolleranti all'amfotericina o all'itraconazolo e fluconazolo, candidosi invasiva in pazienti refrattari o intolleranti all'amfotericina o all'itraconazolo e fluconazolo, candidosi orofaringea (anche come prima scelta), trattamento empirico delle infezioni sistemiche micotiche in pazienti neutropenici . Candidosi invasiva nel neonato qualora gli antimicotici approvati per questa età risultino inefficaci o non tollerati	<p>Walsh TJ, Adamson PC, Seibel NL, Flynn PM, Neely MN, Schwartz C, Shad A, Kaplan SL, Roden MM, Stone JA, Miller A, Bradshaw SK, Li SX, Sable CA, Kartsonis NA. Pharmacokinetics, safety, and tolerability of caspofungin in children and adolescents. <i>Antimicrob Agents Chemother.</i> 2005 Nov;49(11):4536-45</p> <p>Smith PB, Steinbach WJ, Cotten CM, et al. Caspofungin for the treatment of azole resistant candidemia in a premature infant. <i>J Perinatol</i> 2007; 27:127-9.</p> <p>Castagnola E, Franceschi A, Natalizia AR, Mantero E, Tuo P. Combined antifungal therapy in persistent central venous catheter-related candidemia in extremely low birth weight neonates. <i>J Chemother in press.</i></p> <p>Steinbach WJ, Benjamin DK. New antifungal agents under development in children and neonates. <i>Curr Opin Infect Dis</i> 2005;18:484-89.</p> <p>Lehrnbecher T, Groll AH. Experiences with the use of caspofungin in paediatric patients. <i>Mycoses</i> 2008;51(suppl 1):58-64;</p> <p>Merlin E, et al. Efficacy and safety of caspofungin therapy in children with invasive fungal infections. <i>Pediatr Infect Dis J</i> 2006;25:1186-88.</p> <p>Groll AH, et al. Treatment with caspofungin in immunocompromised paediatric patients: a multicenter study.</p> <p>Zautis TE, et al. A prospective, multicenter study of caspofungin for the treatment of documented <i>Candida</i> or <i>Aspergillus</i> infections in paediatric patients. <i>Pediatrics</i> 2009;123:877-84.</p> <p>Odio CM, et al. Caspofungin therapy of neonates with invasive candidiasis. <i>Pediatr Infect Dis J</i> 2004;23:1093-97;</p> <p>Natarajan G, et al. Experience with caspofungin in the treatment of persistent fungemia in neonates. <i>J Perinatol</i> 2005;25:7707-77.</p>
FAMCICLOVIR	Trattamento della infezioni da Herpes Zoster; trattamento delle infezioni da Herpes genitalis primario	Saez-Llorens X et al. Pharmacokinetics and safety of famciclovir in children with herpes simplex or varicella zoster virus infection. <i>Antimicrob Agents Chemother</i> 2009; mar 2009 (epub)

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	e ricorrente e per la soppressione delle recidive da Herpes genitalis; trattamento di pz immunocompromessi affetti da infezioni da Herpes zoster o Herpes simplex. Autorizzare sopra i 12 anni	Ahmed AM et al. Managing herpes zoster in immunocompromised patients. Herpes 2007; 14 (2): 32-36 Dekker C et al. Pediatric use of valacyclovir, penciclovir and famciclovir. Pediatr Infect Dis J 2001; 20 (11): 1079-1081
VALACICLOVIR	Nei pz immunocompetenti: trattamento delle infezioni da virus Varicella-Zoster, trattamento delle infezioni muco-cutanee acute e recidivanti da Herpes simplex, compreso l'Herpes genitale primario o recidivante; soppressione delle recidive da Herpes simplex. Nei pazienti immunodepressi: trattamento delle infezioni da Herpes simplex e Varicella-Zoster; profilassi delle infezioni da Herpes simplex. Indicato per la profilassi delle infezioni da CMV a seguito di trapianto d'organo Indicazione sopra i 2 anni	Boomgaars L et al. Valacyclovir and acyclovir pharmacokinetics in immunocompromised children. Pediatr Blood Cancer 2008; 51 (4): 504-508 Bueno J et al. Current management strategies for the prevention and the treatment of cytomegalovirus infection in pediatric transplant recipients. Pediatr Drugs 2002; 4 (5): 279-290 Dekker C et al. Pediatric use of valacyclovir, penciclovir and famciclovir. Pediatr Infect Dis J 2001; 20 (11): 1079-1081
LAMIVUDINE	Epatite B cronica	Kurbegov Ac, Sokol RS. Hepatitis B therapy in children. Expert Rev. Gastroenterol 2009 Feb; 3 (1): 39-49; Jonas M.M., Little N.R., Gardner S.D. and members of the international pediatric lamivudine investigator group. Long term lamivudine treatment of children with chronic hepatitis B: durability of therapeutic responses and safety. Journal of viral hepatitis. 2008,15, 20-27; Sokal EM, Kelly DA, Mizerski J et al . Long term lamivudine therapy for children with HbeAg-positive chronic Hepatitis B. Hepatology 2006; 43:225-232.
AMANTADINE	Fatica nella sclerosi multipla	Pucci E, Braras P, D'Amico R et al. Amantidine for fatigue in multiple sclerosis. Cochrane Database Syst Rev 2007 Jan 24(1). La gestione della sindrome influenzale. ISS maggio 2008; (adulti e bambini) Scott A. Harper,1 John S. Bradley,2,3 Janet A. et al. Seasonal Influenza in Adults and Children—Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management: Clinical Practice Guidelines of the Infectious Diseases Society of America. Clinical Infectious Diseases 2009; 48:1003–32
INTERFERONE ALFA 2 A PEGINTERFERONE ALFA 2 A	Leucemia mieloide cronica Epatite B cronica	Choe BH, Lee JH, Jang YC. long- term therapeutic efficacy of lamivudine compared with interferon alpha in children with chronic Epatitis B: the younger the better. J Pediatr Gastroenterol Nutr 2007 Jan 44 (1): 92-98.
PEGINTERFERONE ALFA 2a	terapia epatite cronica C nei bambini	Murray KF, Rodrigue J, Gonzalez Peralta R et al. Design of the PEDS-C trial: pegylated interferon +/- ribavirin for children with chronic hepatitis C viral infection. Clinical Trials 2007; 4:661-673.;

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		Schwartz KB, Mohan P, Narkewicz MR. Safety , efficacy and pharmacokinetics of peginterferon alfa 2a in children with chronic hepatitis C. J of gastroent and nutrition , vol 43, no4. october 2006
INTERFERON ALFA 2 B PEGINTERFERONE ALFA 2 A	trattamento epatite cronica B	Boxall EH, Sira J, Ballard AL. Long term follow up of hapatitis B carrier children trated with interferon and prednisolone. J Med Virol 2006 Jul; (78)7; 888-95. Hsu HY, Tsai HY, WU TC. Interferon-alpha in children and young adults with chronic hepatitis B: along term follow-up study in twain. Liver Int 2008 nov; 28 (9).
PEGINTERFERON ALFA 2B PEGINTERFERONE ALFA 2 A	Trattamento epatite C nei bambini. Trattamento epatite B.	Murray KF, rodrigue J, Gonzalez Peralta R e al. Design of the PEDS-C trial: pegylated interferon +/-ribavirin for children with chronic hepatitis C viral infection. Clinical Trials 2007; 4:661-673; Wirth S, Pieper-Boustani H, Lang Thomas. Peginterferon alfa 2 b plus ribavirina treatment in children and adolescents with Chronic Hepatitis C.Hepatology may 2005. Hong Zhao, Fuat Kurbanov, Mo Bin Wan. Genotype B and Younger Patient Age Associated with Better Response to Low Dose Therapy: A Trial with Pegylated/Nonpegylated Interferon α -2b for Hepatitis B e Antigen-Positive Patients with Chronic Hepatitis B in China.Clinical Infectious Diseases 2007;44:541-548.