FARMACI CON USO CONSOLIDATO NELLE CURE PALLIATIVE (FASE DI TERMINALITA') IN PEDIATRIA PER INDICAZIONI ANCHE DIFFERENTI DA QUELLE PREVISTE DAL PROVVEDIMENTO DI AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO
FARE RIFERIMENTO AL DOCUMENTO "FARMACI OFF-LABEL IN CURE PALLIATIVE (CP) PER LA POPOLAZIONE PEDIATRICA" www.aifa.gov.it

Nome principio attivo	*Indicazione terapeutica off-label*	*Referenze di letteratura*
Butilscopolamina-ioscina butilbromuro	Somministrazione e.v. per ostruzione intestinale da peritonite in pazienti oncologici.	Tytgat GN. *Hyoscine butylbromide: a review of its use in the treatment of abdominal cramping and pain*. Drugs 2007 Mercadante S. et al, *Medical treatment for inoperable malignant bowel obstruction: a qualitative systematic review*. J Pain Symptom Manage. 2007 Miller M. and Karwacki M., Management of the gastrointestinal tract in paediatric palliative medicine. OXFORD TEXBOOK OF PALLIATIVE CARE FOR CHILDREN . Oxford University press 2nd edition 2012.
	Somministrazione e.v per riduzione delle secrezioni e del rantolo nella terminalità.	Albert RH. *End-of-Life Care: Managing Common Symptoms*. Am Fam Physician. 2017 Miller M. and Karwacki M., Management of the gastrointestinal tract in paediatric palliative medicine. OXFORD TEXBOOK OF PALLIATIVE CARE FOR CHILDREN . Oxford University press 2nd edition 2012.
Desmedetomidina	Controllo dei sintomi stressanti da patologia o procedura, e difficoltà di addormentamento al di fuori della terapia intensiva in pazienti in cure palliative, come trattamenro in situazioni non	Mahmoud M. et al, *Dexmedetomidine: review, update, and future considerations of paediatric perioperative and periprocedural applications and limitations*. Br J Anaesth. 2015

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	rispondenti alle terapie convenzionali.	Sulton C. et al, *Pediatric Procedural Sedation Using Dexmedetomidine: A Report From the Pediatric Sedation Research Consortium*. Hosp Pediatr. 2016 Ni J. et al, *Effect of dexmedetomidine on preventing postoperative agitation in children: a meta-analysis*. PLoS One. 2015 Weerink M.A.S. et al, *Clinical Pharmacokinetics and Pharmacodynamics of Dexmedetomidine*. Clin Pharmacokinet 2017 Alexopoulou C. et al, *Effects of Dexmedetomidine on Sleep Quality in Critically Ill Patients*. Anesthesiology 2014
	Via di somministrazione endonasale.	Cozzi G. et al, *Intranasal Dexmedetomidine for Procedural Sedation in Children, a Suitable Alternative to Chloral Hydrate*. Paediatr Drugs. 2017
Fentanile	Uso per via transcutanea/endovenosa per la gestione del dolore acuto e/o cronico da patologia oncologica e non oncologica.	Collins J.J. et al, *Transdermal Fentanyl in children with cancer pain: feasibility, tolerability and pharmacokinetic correlates*. J pediatr 1999 Finkel J.C. et al, *Transdermal Fentanyl in the management of children with chronic severe pain*. Cancer 2005 Zernikow B. et al, *Transdermal Fentanyl in childhood and adolescence: a comprensive Literature review*. J Pain 2007 Drake R. et al, Pharmacological management. OXFORT TEXBOOK OF PALLIATIVE CARE FOR CHILDREN . Oxford University press 2006

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	Uso transmucoso per dolore incidente/breakthroug pain/dolore procedurale.	Zernikow B. et al, *Pediatric palliative care: use of opioids for the management of pain*. Paediatr Drugs. 2009 Mystakidou K. et al, *Oral transmucosal fentanyl citrate: overview of pharmacological and clinical characteristics*. Drug Deliv. 2006 Friedrichsdorf S.J. et al, *Management of breakthrough pain in children with cancer*. J Pain Research 2014 Zeppetella G. et al, *Opioids for the management of breakthrough pain in cancer patients*. Cochrane Database Syst Rev. 2013 Drake R. et al, *Pharmacological approaches to pain: Simple analgesics and opioids*. OXFORD TEXBOOK OF PALLIATIVE CARE FOR CHILDREN. Oxford University press 2nd edition 2012
Gabapentin	Dolore neuropatico o misto in bambini in cure palliative, di età superiore a 2 anni.	Friedrichsdorf S.J. et al, *Pain reporting and analgesia management in 270 children with a progressive neurologic, metabolic or chromosomally based condition with impairment of the central nervous system: cross-sectional, baseline results from an observational, longitudinal study*. J Pain Res. 2017 Brown S.C. et al, *A randomized controlled trial of amitriptyline versus gabapentin for complex regional pain syndrome type I and neuropathic pain in children*. Scandinavian Journal of Pain 2016 Cooper T.E., *Antiepileptic drugs for chronic non-cancer pain in children and adolescents*. Cochrane Database Syst

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		Rev. 2017 Kaul I. et al, *Use of gabapentin and pregabalin for pruritus and neuropathic pain associated with major burn injury: A retrospective chart review*. Burns. 2017 Butkovic D. et al, *Experience with gabapentin for neuropathic pain in adolescents: report of five cases*. Paediatr Anaesth. 2006 Mc Cullock R. *Pharmacological approaches to pain. 3: Adjuvants for neuropathic and bone pain*. OXFORD TEXBOOK OF PALLIATIVE CARE FOR CHILDREN . Oxford University press 2nd edition 2012.
Ketamina	Gestione del dolore procedurale o neuropatico/misto non rispondente ad altra terapia, da solo o in associazione/sostituzione ad analgesici oppioidi.	Bredlau A.L. et al, *Oral ketamine for children with chronic pain: a pilot phase 1 study*. J Pediatr. 2013 Bredlau A.L. et al, *Ketamine for pain in adults and children with cancer: a systematic review and synthesis of the literature*. Pain Med. 2013 Tawfic Q.A, A review of the use of ketamine in pain management. J Opioid Manag. 2013 Grunwell J.R. et al, *Pediatric Procedural Sedation Using the Combination of Ketamine and Propofol Outside of the Emergency Department: A Report From the Pediatric Sedation Research Consortium*. Pediatr Crit Care Med. 2017
	Somministrazione per via endonasale.	Poonai N. et al, *Intranasal ketamine for procedural sedation and analgesia in children: A systematic review*. PLoS One. 2017

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		Mehran M. et al, *Effect of Intranasal Sedation Using Ketamine and Midazolam on Behavior of 3-6 Year-Old Uncooperative Children in Dental Office: A Clinical Trial*. J Dent (Tehran). 2017 Scheier E. et al, *Intranasal ketamine proved feasible for pain control in paediatric care and parental support was high*. Acta Paediatr. 2017 Carr D.B. et al, *Safety and efficacy of intranasal ketamine for the treatment of breakthrough pain in patients with chronic pain: a randomized, double-blind, placebo-controlled, crossover study*. Pain. 2004
Ketorolac	Somministrazione orale e sublinguale per un periodo massimo di 5 giorni in soggetti di 4-15 anni di età senza accesso vascolare, per gestione di dolore acuto nocicettivo episodico moderato/severo, quale integrazione di altra analgesia se non efficace.	Dancel R. et al, *Acute Pain Management in Hospitalized Children.* Rev Recent Clin Trials. 2017 Plapler P.G. et al, *Double-blind, randomized, double-dummy clinical trial comparing the efficacy of ketorolac trometamol and naproxen for acute low back pain*. Drug Des Devel Ther. 2016 Neri E. et al, *Sublingual ketorolac versus sublingual tramadol for moderate to severe post-traumatic bone pain in children: a double-blind, randomised, controlled trial*. Arch Dis Child 2013 Di Massa A. et al, *Ketorolac for paediatric postoperative pain. A review*. Minerva Anestesiol. 2000 Marzuillo P. et al, *Narrative review shows that the short-term use of ketorolac is safe and effective in the management of moderate-to-severe pain in children*. Acta Paediatr 2017

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Lidocaina	Uso in aerosol per il trattamento della tosse refrattaria ad altre terapie, in caso di metastasi polmonari.	Slaton R.M. et al, *Evidence for therapeutic uses of nebulized lidocaine in the treatment of intractable cough and asthma*. Ann Pharmacother. 2013 Decco M.L. et al, *Nebulized lidocaine in the treatment of severe asthma in children: a pilot study*. Ann Allergy Asthma Immunol. 1999 Truesdale K. et al, *Nebulized lidocaine in the treatment of intractable cough*. Am J Hosp Palliat Care. 2013 Molassiotis A. et al, *Symptomatic Treatment of Cough Among Adult Patients With Lung Cancer: CHEST Guideline and Expert Panel Report*. Chest. 2017
	Uso endovenoso per il trattamento del dolore neuropatico in pazienti in cure palliative non rispondenti alle terapie convenzionali.	Hutson P. et al, *Intravenous lidocaine for neuropathic pain: a retrospective analysis of tolerability and efficacy*. Pain Med. 2015 Kajiume T. et al, *Continuous intravenous infusion of ketamine and lidocaine as adjuvant analgesics in a 5-year-old patient with neuropathic cancer pain*. J Palliat Med. 2012
Midazolam	Uso intranasale per minore invasività e rapidità di somministrazione in assenza di accesso venoso, anche in caso di urgenza in pazienti in cure palliative di età superiore a 1 mese.	Tsze D.S. et al, *Optimal Volume of Administration of Intranasal Midazolam in Children: A Randomized Clinical Trial*. Ann Emerg Med. 2017 Nemeth M. et al, *Intranasal Analgesia and Sedation in Pediatric Emergency Care-A Prospective Observational Study on the*

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		Implementation of an Institutional Protocol in a Tertiary Children's Hospital. Pediatr Emerg Care. 2017 Jain P. et al, *Efficacy and safety of anti-epileptic drugs in patients with active convulsive seizures when no IV access is available: Systematic review and meta-analysis*. Epilepsy Res. 2016 Glauser T. et al, *Evidence-Based Guideline: Treatment of Convulsive Status Epilepticus in Children and Adults: Report of the Guideline Committee of the American Epilepsy Society*. Epilepsy Curr. 2016 Chiaretti A. et al, *Intranasal lidocaine and midazolam for procedural sedation in children*. Arch Dis Child. 2011
	Uso endovenoso per la gestione di sintomi da distress non doloroso nella fase di terminalità.	Korzeniewska-Eksterowicz A. et al, Palliative sedation at home for terminally ill children with cancer. J Pain Symptom Manage. 2014 Postovsky S. et al, *Practice of palliative sedation in children with brain tumors and sarcomas at the end of life*. Pediatr Hematol Oncol. 2007 Cowan J.D. et al, *Terminal sedation in palliative medicine--definition and review of the literature*. Support Care Cancer. 2001 Wolfe J. et al, *Textbook of interdisciplinary pediatric palliative care*. Elsevier Saunders 2011
Ondansetron	Controllo della nausea e del vomito in corso di terapia con oppioidi in pazienti in cure palliative in età ≥ 6 mesi.	Jitpakdee T. et al, *Strategies for preventing side effects of systemic opioid in postoperative pediatric patients*. Paediatr Anaesth 2014

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		Engelman E. et al, *How much does pharmacologic prophylaxis reduce postoperative vomiting in children? Calculation of prophylaxis effectiveness and expected incidence of vomiting under treatment using Bayesian meta-analysis*. Anesthesiology 2008 Gomez-Arnau J.I. et al, *Postoperative nausea and vomiting and opioid-induced nausea and vomiting guidelines for prevention and treatment*. Rev Exp Anestesiol Reanim 2010 Culy C.R. et al, *Ondansetron: a review of its use as an antiemetic in children*. Paediatr Drugs 2001 Binstock W. et al, *The effect of premedication with OTFC, with or without ondansetron, on postoperative agitation, and nausea and vomiting in pediatric ambulaotry patients*. Pediatr Anesthesia 2004
Scopolamina/ ioscina idrobromuro	Trattamento della scialorrea in pazienti in cure palliative e in fine vita.	Bavikatte G. et al, *Management of Drooling of Saliva*. BJMP 2012 Mato A. et al, *Management of drooling in disabled patients with scopolamine patches*. BJCP 2010 Little S.A. et al, *An evidence-based approch to the child who drools saliva*. Clin Otolaryngology 2009 Táboas-Pereira M.A. et al, *Drooling therapy in children with neurological disorders*. Rev Neurol. 2015 Jongerius P.H. et al, *Effect of botulinum toxin in the treatment of*

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		drooling: a controlled clinical trial. Pediatrics. 2004 Walshe M. et al, *Interventions for drooling in children with cerebral palsy*. Cochrane Database Syst Rev. 2012 Chowdhury N.A. et al, *Transdermal Scopolamine Withdrawal Syndrome Case Report in the Pediatric Cerebral Palsy Population*. Am J Phys Med Rehabil. 2017 Delgado-Charro M.B. et al, *Effective use of transdermal drug delivery in children*. Adv Drug Deliv Rev. 2014 Miller M. et al, Management of the gastrointestinal tract in paediatric palliative medicine. OXFORD TEXBOOK OF PALLIATIVE CARE FOR CHILDREN . Oxford University press 2nd edition 2012