Pediatric Pharmacotherapeutics 2022: Children Are Not Little Adults!

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OWNER: PARTNERS IN HEALTHCARE EDUCATION, LLC

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Objectives

- Upon completion of this program, the participant will be able to:
  - Identify ways in which children are different than adults in terms of pharmacotherapeutics
  - Discuss common pediatric prescribing errors
  - Discuss strategies to prevent pediatric prescribing errors
  - Identify medications with new pediatric approvals

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Disclosures

- Speaker Bureau:
  - Sanofi-Pasteur, Merck, Pfizer: Vaccines
  - AbbVie and Biohaven: Migraines
  - Idorsia: Insomnia
- Consultant:
  - Sanofi-Pasteur, Merck, Pfizer, Moderna, and Seqirus: Vaccines
  - GlaxoSmithKline: OA and Pain
  - Bayer: Chronic Kidney Disease
  - Idorsia: Insomnia
  - Shield Therapeutics: Iron Deficiency Anemia

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Why are we here today?

- 200,000 medication errors are reported to U.S. poison-control centers; approximately 30% of these errors involve children
- Dosing errors constitute the biggest errors
- Why are there issues:
  - Most medications used in the care of children are formulated and packaged primarily for adults.
  - Most health care settings are primarily built around the needs of adults.
  - Children—especially young, small and sick children—are usually less able to physiologically tolerate a medication error due to still developing renal, immune and hepatic functions
  - Many children, especially very young children, cannot communicate effectively to providers regarding any adverse effects that medications may be causing

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https://www.uspharmacist.com/article/minimizing-medication-errors-in-pediatric-patients accessed 01-20-2021

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Medication development

- Until the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), most medications were not developed or even tested initially in children
  - There is no reliable formula to convert adult dosages to those which are safe or effective in children
  - When manufacturers do not test drugs in infants and children, it has led to disastrous results
    - Gray baby syndrome: chloramphenicol in children
    - Sulfonamide-induced kernicterus in newborns

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Goodman, Louis S., Alfred Gilman, Joel G. Hardman, Alfred Goodman Gilman, and Lee E. Limbird. *Goodman & Gilman's the pharmacological basis of therapeutics*. 9th ed. New York: McGraw-Hill, Health Professions Division, 1996. Print.

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Pediatric studies and approvals

- The Pediatric Research Equity Act (PREA) mandates that almost all new medicines be studied in children if pediatric use of the product is likely
- In addition, the Best Pharmaceuticals for Children Act (BPCA) opens the door for an additional 6 months of market exclusivity for sponsors that submit completed pediatric studies to the FDA

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http://www.medscape.com/viewarticle/820978 accessed 07-01-2014

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FDA approval of medications in children

- 25% of all of the drugs approved by the FDA have any specific indications for children
- In the past 10 years, 12% of all prescriptions written in the US were prescribed for children < 9 years of age

Gutierrez, Kathleen, and Sherry F. Queener. *Pharmacology for nursing practice*. St. Louis: Mosby, 2003

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Pediatric Medication Errors

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Children: Are they different?

- Children differ from adults:
  - Drug absorption
  - Distribution
  - Biotransformation
  - Excretion/Elimination

Gutierrez, Kathleen, and Sherry F. Queener. *Pharmacology for nursing practice*. St. Louis: Mosby, 2003

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Absorption

- Most orally administered medications are absorbed in the small intestine
  - Infants have proportionately larger small intestinal surface areas, this can lead to unpredictable absorption when compared with adults
- Infants also have increased intestinal motility, which alters the absorption of drugs with limited water solubility, such as phenytoin (Dilantin) and carbamazepine (Tegretol)

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What about topical medications?

- Newborns and infants have greater skin absorption - due to increased hydration and thinner stratum corneum than adults
- Systemic toxicity can occur with relatively small amounts of topical application of medications such as diphenhydramine (Benadryl and many other products), lidocaine, corticosteroids and hexachlorophene (PhisoHex)
- **Caution with prescribing topical medications**

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Actual example

- Pediatric studies led to relabeling of betamethasone dipropionate (Diprolene, Diprosone) and betamethasone dipropionate-clotrimazole (Lotrisone)
  - These studies documented hypothalamic-adrenal axis suppression in 23% to 73% of pediatric patients depending on formulation used

Roberts R, Rodriguez W, Murphy D, Crescenzi T. Pediatric drug labeling: improving the safety and efficacy of pediatric therapies. *JAMA*. 2003;290:905-911.

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Children: Drug clearance pathways

- Most drug clearance pathways develop over the first year of life
  - Although not all pathway development is fully known in children, most develop by 1 year
  - For instance:
    - CYP1A2 pathway, studies were performed in children using caffeine which showed that by year one the pathway is developed.
    - Important: if drugs such as theophylline which also used this pathway are administered before 1 year, significant toxicity occurs
    - At puberty, clearance begins to decline

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Goodman, Louis S., Alfred Gilman, Joel G. Hardman, Alfred Goodman Gilman, and Lee E. Limbird. *Goodman & Gilman's the pharmacological basis of therapeutics*. 9th ed. New York: McGraw-Hill, Health Professions Division, 1996. Print.

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CYP450 pathways and children

Activity in Enzyme	Fetus/Neonate	Age Adult Level Achieved
CYP1A2	Nearly absent	4 months
CYP2C	Nearly absent	6 months
CYP2D6	Nearly absent	3-5 years
CYP3A4	Low	6-12 months
CYPP3A7	High	Declines in first week of life; not present in adults

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Gutierrez, Kathleen, and Sherry F. Queener. *Pharmacology for nursing practice*. St. Louis: Mosby, 2003

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Important take away

- 7 day neonate will be very different from a pharmacokinetic perspective than a newborn
- The dosage that is appropriate for a 10 year old may be an overdose for a 16 year old
- All dosages need to be checked for age and weight repeatedly

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What Medications Are Involved in Most Pediatric Outpatient Prescribing Errors?

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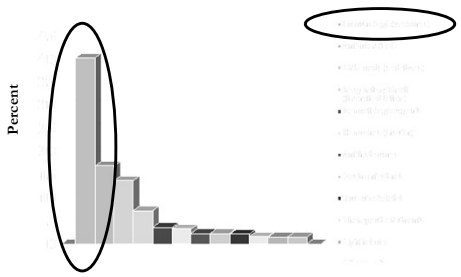
Results: Medications Involved



https://www.google.com/search?newwindow=1&site=&source=hp&q=pediatric+prescriptions&oq=pediatric+prescriptions&gs_l=hp.3..0j0i22i30l8.1146.6430.0.7963.23.17.0.6.6.0.144.1907.4j13.17.0....0...1c.1.48.hp..0.23.1993.Ph2SE2iWdpA
Accessed 07-01-2014

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Important take away

- Two people should check vaccine record prior to administration of vaccines, if possible
- Two people should look at actual vaccine prior to administration, if possible

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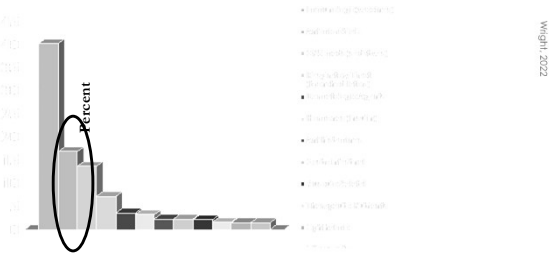
Results: Medications Involved



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https://www.google.com/search?newwindow=1&site=&source=hp&q=pediatric+prescriptions&oq=pediatric+prescriptions&gs_l=hp.3..0j0i22i30l8.1146.6430.0.7963.23.17.0.6.6.0.144.1907.4j13.17.0....0...1c.1.48.hp..0.23.1993.Ph2SE2iWdpA
Accessed 07-01-2014

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Dosing medications in children

- Most medications are dosed by mg/kg/day
  - However, there are many drugs which are reported as total dosage vs. others which are dosed two – three times daily
  - 1 kg = 2.2 pounds
- Double check your references
  - Epocrates
  - Lexi-Comp
  - http://www.empr.com/pediatrics-edition/section/1299/

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Reasons for errors: Recommended doses can differ

Source	Recommended pediatric dose for oxycodone
Harriet Lane Handbook	0.2 to 0.9 mg/kg/day q 4-6 hours
HMO Formulary	No weight-based dose provided.
Children's Hospital Formulary	0.2 to 1.6 mg/kg/day q 3-4 hours

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Doses may be higher in children: amoxicillin

6 year-old 40kg male with otitis failed conservative therapy

↓

Amoxicillin 90 mg/kg/day divided bid

↓	↓
Appropriate pediatric dose:	Appropriate adult dose:
3600 mg/day (1800mg bid)	2000 mg/day (1000 bid)

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General techniques to avoid prescribing errors

- Clear writing and documentation
  - EHR, if available
- Double check dosages
- Avoid writing RX's when patient is talking to you or sitting in front of you
- Have a list of high-risk medications; when you see this list – bells should go off in your head
- Double check interactions

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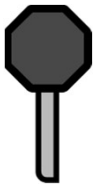
DO NOT DEVELOP EHR ALERT FATIGUE



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Additional elements of safe prescription writing

- Include diagnosis on prescription
- Many prescriptions now enable provider to write kg or weight on RX
- Never write a prescription without a 0 or number before the decimal point
  - For instance: 0.5 milligrams
- Never put a zero after a decimal point
  - For instance: 10 milligrams NOT 10.0 mg
- Always calculate out the amount of the total medication needed
  - This serves as a double check system
  - 10 mL two times daily x 10 days = 200 Ml
  - Do not write quantity sufficient

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Pediatric Medication Adherence

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Factors affecting medication adherence

- Frequency of dosing
- Palatability
- Route of administration
- Cost
- Administration instructions

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Adherence to Medication Regimens

- Adherence to a regimen decreases as the frequency of a drug increases
  - In an NIH published trial, mean dose-taking compliance was 71% +/- 17% (range, 34%-97%) and declined as the number of daily doses increased
  - For instance: 1 dose = 79% +/- 14%, 2 doses = 69% +/- 15%, 3 doses = 65% +/- 16%, 4 doses = 51% +/- 20% (P < 0.001 among dose schedules)
  - Compliance was significantly higher for once-daily versus 3-times-daily (P = 0.008), once-daily versus 4-times-daily (P < 0.001), and twice-daily versus 4-times-daily regimens (P = 0.001)

Claxton, A. J., Cramer, J., & Pierce, C. (2001). A systematic review of the associations between dose regimens and medication compliance. Clinical Therapeutics, 23(8), 1296-1310.

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Children: Palatability

- Another issue which significantly affects medication utilization in children is taste and palatability
- This is more so in pediatrics than any other age group

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Flavoring is routinely available

- In general, the following medications have poor taste
  - Penicillins
  - Prednisone
  - Clindamycin
  - Azithromycin
  - Trimethoprim/sulfamethosazole
- Better tasting:
  - Cephalosporins

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Length of Prescriptions

- Increasing trend to decrease length of prescriptions
- Recent studies have shown that for most conditions in children, shorter courses may provide same benefits, often with fewer side effects and better adherence

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Duration of treatment for AOM

- Results
  - 10 days: Patients <2 years old or those with severe symptoms
  - 7 days: Age 2-5 years of age with mild – moderate AOM
  - 5 – 7 days: 6 years and older with mild – moderate symptoms

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556
accessed 05-01-2013

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Specific Medications and Warnings in Pediatrics

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Cough and cold medications in children

Public Health Advisory: FDA Recommends that Over-the-Counter (OTC) Cough and Cold Products not be used for Infants and Children under 2 Years of Age

http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/drugsafetyinformationforheathcareprofessionals/publichealthadvisories/ucm051137.htm accessed 07-01-2014

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Acetaminophen vs. Ibuprofen vs. Aspirin

- Acetaminophen dosage:
  - 10-15 mg/Kg/dose q 4-6 hours
  - Max 5 doses in 24 hours
- Ibuprofen dosage:
  - 5-10 mg/Kg/dose q 6-8 hours
  - Max OTC dosing 40 mg/Kg/day OR 1.2 Gm/day
- What about aspirin?
  - NONE < 19 YEARS DUE TO RISK OF REYE'S SYNDROME
  - Keep in mind that many products contain salicylates

http://www.aafp.org/afp/2009/1215/p1472.html accessed 07-01-2014

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Stevens-Johnson Syndrome

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- August 1, 2013 – Acetaminophen: The U.S. Food and Drug Administration (FDA) notified healthcare professionals and patients that acetaminophen has been associated with a risk of rare but serious skin reactions. Acetaminophen is a common active ingredient to treat pain and reduce fever; it is included in many prescription and over-the-counter (OTC) products. These skin reactions, known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP), can be fatal. These reactions can occur with first-time use of acetaminophen or at any time while it is being taken. Other drugs used to treat fever and pain/body aches (e.g., non-steroidal anti-inflammatory drugs, or NSAIDS, such as ibuprofen and naproxen) also carry the risk of causing serious skin reactions, which is already described in the warnings section of their drug labels.

http://www.guideline.gov/content.aspx?id=38416&search=strep+pharyngitis Accessed 07-01-2014

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Specific Pediatric Conditions

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Allergic rhinitis

- Many OTC medications are available
- Caution:
  - First generation antihistamines
  - Anticholinergic effects
    - Sedation or agitation
    - Tachycardia
    - Dry mouth
    - Urinary retention
- Examples:
  - Diphenhydramine
  - Chlorpheniramine

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Allergic Rhinitis

- Recommendations for pediatrics
  - 2nd generation antihistamines are available OTC
  - Fewer side effects than first generation antihistamines
  - Have dosages and formulations available for children
  - Examples:
    - Loratadine (Claritin, Alavert): 2-5 years of age and > 6 years (adjust dosing with renal impairment)
    - Cetirizine (Zyrtec):
      - Children's Zyrtec Allergy: 6 – 11 months: 2.5 ML po daily prn;
      - 12-23 months: 2.5 ML once – two times daily prn;
      - 2-5 years of age: 2.5 – 5 mL/day; maximum 5mL/24 hours
      - > 6 years (adjust or avoid with renal impairment): 5 – 10 mL per day or 5 – 10 mg daily
    - Fexofenadine (Allegra): 6 months – 2 years, 2 – 5 years and > 6 years
      - DO NOT GIVE WITH FRUIT JUICE (reduces absorption of drug by > 1/3)

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2020 Focused Updates to the Asthma Management Guidelines: Clinician's Guide

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https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/clinician-guide-2020-focused-updates-asthma-management-guidelines

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Ages 0 – 4 years

2020 FOCUSED UPDATES TO THE Asthma Management Guidelines | CLINICIAN'S GUIDE

AGES 0–4 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 0–4 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA and At the start of RTI: Add short course daily ICS▲	Daily low-dose ICS and PRN SABA	Daily low-dose ICS-LABA and PRN SABA▲ or Daily low-dose ICS + montelukast,* or daily medium-dose ICS, and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily montelukast* or Cromolyn,* and PRN SABA		Daily medium-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast*+ oral systemic corticosteroid and PRN SABA
			For children age 4 years only, see Step 3 and Step 4 on Management of Persistent Asthma in Individuals Ages 5–11 Years diagram.			

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 4–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 3 or higher is required. Consider consultation at Step 2.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; SABA, inhaled short-acting beta$_2$-agonist; RTI, respiratory tract infection; PRN, as needed

▲ Updated based on the 2020 guidelines.

* Cromolyn and montelukast were not considered for this update and/or have limited availability for use in the United States. The FDA issued a Boxed Warning for montelukast in March 2020.

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Ages 5 – 11 years

2020 FOCUSED UPDATES TO THE Asthma Management Guidelines | CLINICIAN'S GUIDE

AGES 5–11 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 5–11 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily LTRA,* or Cromolyn,* or Nedocromil,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LTRA,* or daily low-dose ICS +Theophylline,* and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA or Daily medium-dose ICS + LTRA* or daily medium-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* or daily high-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* + oral systemic corticosteroid or daily high-dose ICS + Theophylline* + oral systemic corticosteroid, and PRN SABA
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider Omalizumab**▲	

Assess Control

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Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

▲ Updated based on the 2020 guidelines.

* Cromolyn, Nedocromil, LTRAs including montelukast, and Theophylline were not considered in this update and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a Boxed Warning for montelukast in March 2020.

** Omalizumab is the only asthma biologic currently FDA-approved for this age range.

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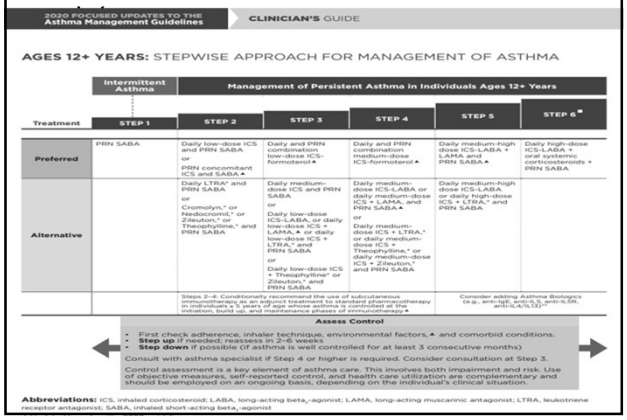
Ages 12 years and



2020 FOCUSED UPDATES TO THE Asthma Management Guidelines — CLINICIAN'S GUIDE

AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

Treatment	Intermittent Asthma: STEP 1	Management of Persistent Asthma in Individuals Ages 12+ Years: STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA▲	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily medium-high dose ICS-LABA + LAMA and PRN SABA▲	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA,▲ or daily low-dose ICS + LTRA,* and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA	Daily medium-dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA▲ or Daily medium-dose ICS + LTRA,* or daily medium-dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA	
		Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy for patients who have allergic asthma. Consider during the initiation, build up, and maintenance phases of immunotherapy.▲			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

Assess Control

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Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

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Asthma exacerbation

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Oral corticosteroids

- Oral corticosteroids
  - Multiple products are available
    - Each product has different flavoring; most taste terrible (consider flavoring)
    - Most are available in 15 mg/5mL
  - Dosage: 1 mg/kg/day – 2 mg/kg/day
    - Split dosing in children is preferred
- Length 3-10 days
  - Average: 5-7 days
  - No taper necessary
- Dosage & effect equivalent between prednisolone (liquid) and prednisone (tablets)

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Antimicrobials

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PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

The Diagnosis and Management of Acute Otitis Media

Allan S. Lieberthal, Aaron E. Carroll, Tasnee Chonmaitree, Theodore G. Ganiats, Alejandro Hoberman, Mary Anne Jackson, Mark D. Joffe, Donald T. Miller, Richard M. Rosenfeld, Xavier D. Sevilla, Richard H. Schwartz, Pauline A. Thomas and David E. Tunkel

Pediatrics; originally published online February 25, 2013;
DOI: 10.1542/peds.2012-3488

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Variations of Tympanic Membrane

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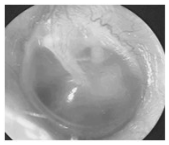
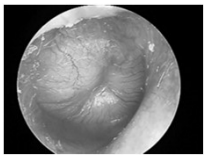
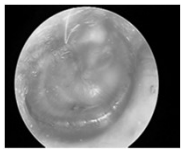
Normal TM



Acute OM



Otitis Media with Effusion



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AAP Updated Guidelines

- Diagnosis of AOM:
  - Evidence: 1A
    - Moderate - severe bulging of TM with otalgia
    - OR…new otorrhea NOT due to otitis externa with otalgia
  - Evidence: 1B
    - Mild bulging of TM and….
      - Recent (< 48 hours) onset of ear pain or….
    - Intense erythema of TM with otalgia

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http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556
accessed 05-01-2013

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Who Needs Antimicrobials

- Any child < 6 months of age
- Any child with severe AOM
- Any child < 24 months of age with bilateral AOM
- Any child in whom follow-up can not be ensured

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AAP Updated Guidelines (cont.)

- Severe AOM:
  - Moderate or severe otalgia OR
  - Pain for at least 48 hours OR…
  - Temperature: 102.2 (39 degrees Celsius)

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http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556
accessed 05-01-2013

51

AAP Updated Guidelines (cont.)

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- Treatment options:
  - Amoxicillin: first line
    - Provided that: no antibiotics in previous 30 days and
    - No purulent conjunctivitis and
    - Not allergic to PCN

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556 accessed 05-01-2013

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AAP Updated Guidelines (cont.)

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- Treatment options:
  - Amoxicillin/clavulanate
    - Child who has received antibiotics in previous 30 days OR….
    - Has concurrent purulent conjunctivitis OR….
    - History of AOM which is unresponsive to amoxicillin

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556 accessed 05-01-2013

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Initial Immediate or Delayed Antibiotic Treatment

Recommended First line Treatment	Alternative Treatment (if Penicillin Allergy)
Amoxicillin (80-90 mg/kg/day) in two divided doses OR	Cefdinir (14 mg/kg/day) in one – two divided doses Cefuroxime (30 mg/kg/day) in two divided doses
Amoxicillin/clavulanate (90 mg/kg/day or amoxicillin) with 6.4 mg/kg/day of clavulanate) in two divided doses	Cefpodoxime (10mg/kg/day) in two divided doses Ceftriaxone (50 mg/kg/day IM or IV) daily for 1 or 3 days

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556 accessed 05-01-2013

54

Antibiotic Treatment After 48-72 hours of Failure of Initial Antibiotic

Recommended First line Treatment	Alternative Treatment (if Penicillin Allergy)
Amoxicillin/clavulanate (90 mg/kg/day or amoxicillin) with 6.4 mg/kg/day of clavulanate) in two divided doses	Ceftriaxone 3 day Clindamycin (30 – 40 mg/kg/day) in three divided doses with or without concomitant third generation cephalosporin
Ceftriaxone (50 mg/kg/day IM or IV) for 3 days	Clindamycin (30 – 40 mg/kg/day) in three divided doses with concomitant third generation cephalosporin Tympanocentesis Consult specialist

http://www.google.com/#sclient=psyab&q=guidelines+on+AOM&oq=guidelines+on+AOM&gs_l=serp.3..0i22i30l2.1956.5384.0.5749.19.13.1.5.5.0.127.1021.11j2.13.0...0.0...1c.1.11.psy-ab.8e640vy70iU&pbx=1&bav=on.2,or.r_qf.&fp=a7cbcbf4ec25b454&biw=1240&bih=556 accessed 05-01-2013

55

Remember…

- For children with OM and tympanostomy tubes:
  - You may also utilize topical medications
  - Ofloxacin (Floxin Otic) 0.3% solution
    - Age 1 - 12 years: 5 drops into affected ear bid x 10 days
  - Ciprofloxacin (Ciprodex):
    - 6 months and up: 4 drops into the affected ear bid x 7 days

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Otitis Media with Effusion

- Fluid in the middle ear
- No signs and symptoms of AOM
  - Air fluid levels
  - Dullness of TM
  - Decreased movement of TM

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http://pediatrics.aappublications.org/cgi/content/abstract/113/5/1412 accessed 02-01-2010

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OME

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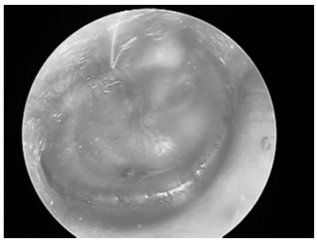

58

OME

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- Treatment:
  - Observation as a treatment option
  - Majority – up to 90% will resolve within 3 months without intervention
  - If still present at 12 weeks – may need hearing evaluation, referral to ENT
  - High risk individuals may be candidates for myringotomy

http://pediatrics.aappublications.org/cgi/content/abstract/113/5/1412 accessed 02-01-2010

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IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults Clinical Infectious Diseases Advance Access published March 20, 2012

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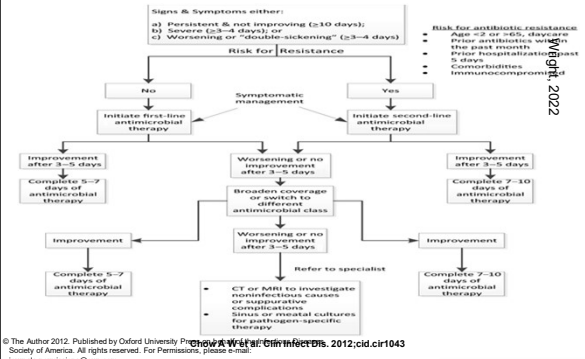
http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
Accessed 12-29-2012

60

Algorithm for the management of acute bacterial rhinosinusitis



Chow A W Eur J Clin Infect Dis. 2012;cid.cir1043

Clinical Infectious Diseases

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61

What Constitutes at Risk for Resistance?

- Age < 2 years or > 65 years
- Daycare
- Antimicrobial within past 1 month
- Hospitalization within past 5 days
- Comorbidities
- Immunocompromised

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
Accessed 12-29-2012

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Goals of Treatment

- Restore integrity and function of osteomeatal complex
  - Reduce inflammation
  - Restore drainage
  - Eradicate bacterial infection

http://www.medscape.com/viewprogram/5621 accessed 01-22-07

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63

Treatment of Acute Bacterial Rhinosinusitis

- Nonpharmacologic Therapies
  - Increased water intake
  - Intranasal saline irrigations with either physiologic or hypertonic saline are recommended as an adjunctive treatment in adults with ABRS[1]

[1]http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html Accessed 12-29-2012

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Management Strategies in ABRS

- Antihistamines or decongestants
  - No longer recommended
- Topical corticosteroids
  - Intranasal corticosteroids are recommended as an adjunct to antibiotics in the empiric treatment of ABRS, primarily in patients with a history of allergic rhinitis[1]

[1]http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html Accessed 12-29-2012

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Antimicrobial Regimens in Children

Table 9. Antimicrobial Regimens for Acute Bacterial Rhinosinusitis in Children

Indication	First-line (Daily Dose)	Second-line (Daily Dose)
Initial empirical therapy	• Amoxicillin-clavulanate (45 mg/kg/day PO bid)	• Amoxicillin-clavulanate (90 mg/kg/day PO bid)
β-lactam allergy		
Type I hypersensitivity		• Levofloxacin (10–20 mg/kg/day PO every 12–24 h)
Non-type I hypersensitivity		• Clindamycin[a] (30–40 mg/kg/day PO tid) plus cefixime (8 mg/kg/day PO bid) or cefpodoxime (10 mg/kg/day PO bid)
Risk for antibiotic resistance or failed initial therapy		• Amoxicillin-clavulanate (90 mg/kg/day PO bid)
		• Clindamycin[a] (30–40 mg/kg/day PO tid) plus cefixime (8 mg/kg/day PO bid) or cefpodoxime (10 mg/kg/day PO bid)
		• Levofloxacin (10–20 mg/kg/day PO every 12–24 h)
Severe infection requiring hospitalization		• Ampicillin/sulbactam (200–400 mg/kg/day IV every 6 h)
		• Ceftriaxone (50 mg/kg/day IV every 12 h)
		• Cefotaxime (100–200 mg/kg/day IV every 6 h)
		• Levofloxacin (10–20 mg/kg/day IV every 12–24 h)

Abbreviations: bid, twice daily; IV, intravenously; PO, orally; qd, daily; tid, 3 times a day.

[a] Resistance to clindamycin (~31%) is found frequently among *Streptococcus pneumoniae* serotype 19A isolates in different regions of the United States [34].

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html accessed 12-29-2012

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Important Changes

- Macrolides (clarithromycin and azithromycin) are not recommended due to high rates of resistance among *S. pneumoniae* (30%)
- TMP/SMX is not recommended due to high rates of resistance among both *S. pneumoniae* and *H. influenzae* (30%–40%)
- Second and third-generation cephalosporins are no longer recommended due to variable rates of resistance among *S. pneumoniae*.

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
accessed 12-29-2012

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Length of treatment

- The recommended duration of therapy for uncomplicated ABRS in adults is 5–7 days
- In children with ABRS, the longer treatment duration of 10–14 days is still recommended

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
Accessed 12-29-2012

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When to Change Treatments

- An alternative treatment should be considered if symptoms worsen after 48–72 hours of initial empiric antimicrobial therapy, or when the individual fails to improve despite 3–5 days of antimicrobial therapy

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html
Accessed 12-29-2012

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When to Refer

Table 14. Indications for Referral to a Specialist

- Severe infection (high persistent fever with temperature >39°C [>102°F]; orbital edema; severe headache, visual disturbance, altered mental status; meningeal signs)
- Recalcitrant infection with failure to respond to extended courses of antimicrobial therapy
- Immunocompromised host
- Multiple medical problems that might compromise response to treatment (eg, hepatic or renal impairment, hypersensitivity to antimicrobial agents, organ transplant)
- Unusual or resistant pathogens
- Fungal sinusitis or granulomatous disease
- Nosocomial infection
- Anatomic defects causing obstruction and requiring surgical intervention
- Multiple recurrent episodes of acute bacterial rhinosinusitis (ABRS) (3-4 episodes per year) suggesting chronic sinusitis
- Chronic rhinosinusitis (with or without polyps or asthma) with recurrent ABRS exacerbations
- Evaluation of immunotherapy for allergic rhinitis

http://cid.oxfordjournals.org/content/early/2012/03/20/cid.cir1043.full.pdf+html Accessed 12-29-2012

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What Does AAP Say?

- Amoxicillin alone or in combination with clavulanate is the first-line antibiotic choice
  - Length of treatment: 5-7 days
- Children with hypersensitivity to amoxicillin (type 1 and non–type 1):
  - cefdinir (Omnicef), cefuroxime (Ceftin), or cefpodoxime (Cefdinir)

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AAP Releases Guideline on Diagnosis and Management of Acute Bacterial Sinusitis in Children One to 18 Years of Age - Practice Guidelines – American Family Physician (aafp.org) accessed 11-28-2020

71

Pharyngitis

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Pharyngitis

- Epidemiology
  - Group A Beta Hemolytic Strep
    - Most interest because of its association with severe complications
    - Peritonsillar abscesses, rheumatic fever, post-streptococcal glomerulonephritis - complications

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Exudative pharyngitis

Exudative pharyngitis
Differentials include:
Strep pharyngitis
Peritonsillar abscess
Mononucleosis
Viral pharyngitis

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Strep pharyngitis treatment

- Penicillin VK 250-500 mg BID X 10 days
  - 250 mg two times daily (children)
  - 500 mg two times daily (adolescents)
  - Amoxicillin 50 mg/Kg/day divided BID X 10 days is acceptable and tastes better in liquid form, but broader spectrum than needed
    - ONCE DAILY is okay option
    - Not to exceed 1000 mg daily of amoxicillin
- Penicillin allergy
  - Past urticaria/anaphylaxis-
    - Erythromycin 50 mg/kg/day, divided BID- 4xDay X 10 days (possible alternatives: Azithromycin X 5 days, clindamycin X 10 days)
  - NOT urticaria/anaphylaxis - Cephalexin possible

Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, Martin JM, Van Beneden C. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clin Infect Dis. 2012 Nov;55(10):e86-e102.accessed 07-01-2014

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Miscellaneous Pediatric Prescribing Information

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Miscellaneous

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- Albuterol inhalers
  - All contain 200 inhalations
  - Well-controlled patients should need < 1 inhaler per year
  - Closely monitor utilization of these inhalers

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Herbal preparations

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- Resurgence of usage of herbal or complementary therapies
  - N-acetyl-methoxytryptamine (Melatonin)
  - Hypericum (St. John's Wort)
  - Echinacea purpurea (Echinacea)
- Significant number of drug/drug interactions
- Many are unsafe in pediatrics
  - Hypericum (St. John's Wort) interacts with a significant number of other medications
  - CYP3A4 inducer

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Miscellaneous Pediatric Approvals

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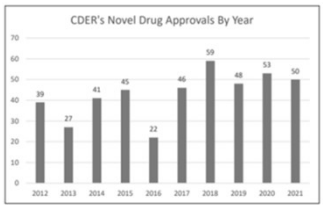

FDA 2022: Center for Drug Evaluation and Research

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Influenza Prophylaxis

- Baloxavir marboxil (Xofluza) approved for postexposure prophylaxis of influenza in persons 12 years of age and older following contact with an individual who has influenza
  - Patient weight < 80 kg (2 – 20 mg for a total of 40 mg)
  - 80 kg or greater (2 – 40 mg tablets for a total of 80 mg)
  - With or without food

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Ivermectin

- Ivermectin 0.5% lotion (Sklice)
  - Now approved OTC for children 6 months of age and older with head lice
  - Does not require combing of nits

82

Minocycline topical (Amzeeq)

- First topical minocycline product for the treatment of moderate – severe acne in individuals 9 years of age and older
  - Available as a foam – 4%
  - Do not use < 9 years of age (bone growth and tooth discoloration)
- Apply to the skin 1 hour prior to bed
  - Do not shower or wash off after application

https://druginserts.com/lib/rx/meds/amzeeq-1/ accessed 01-30-2020

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Minocycline topical

- Avoid in pregnancy or lactation
  - TCNs can cross the placenta when taken orally
- Warnings/side effects
  - Hepatotoxicity has been reported with oral TCN
  - Photosensitivity
  - Tissue hyperpigmentation
  - Headache (3%) vs. 2% of subjects treated with placebo (most common side effect)
- Cost:
  - $592.00 for 1 month

https://druginserts.com/lib/rx/meds/amzeeq-1/ accessed 01-30-2020

84

Additional Approval

- Liraglutide (Victoza): approved for Type 2 diabetes in children: ≥ 10 years of age
- Duloxetine (Cymbalta): approved for fibromyalgia in individuals 13 years of age and older

https://www.fda.gov/media/143552/download accessed 01-20-2021

85

New Approvals

- Tofacitinib (Xeljanz) for patients 2 years and older with active polyarticular juvenile idiopathic arthritis marking the first Janus kinase inhibitor approved for use in children
  - This is an oral treatment
- In May, the FDA approved Solifenacin succinate (Vesicare) for patients 2 years of age and older with bladder dysfunction due to neurogenic detrusor overactivity

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Mepolizumab (Nucala)

- FDA approval for add-on therapy for patients 6 – 11 years of age with severe eosinophilic asthma

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Glucopyrronium (Qbrexza)

- Treatment of primary axillary hyperhidrosis in children 9 years of age and older and adults
- Single-use cloth
- Anti-cholinergic
- Apply once every 24 hours to axillary regions

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New

- Secnidazole (Solosec)
  - Approved for the treatment of trichomoniasis
  - 2 grams as a single dose
  - ALSO, NEW APPROVAL –
    - 12 years of age and older for BV and trichomoniasis
- Azelastine hydrochloride nasal spray, 0.15% approved for OTC sales; individuals 6 and older

https://www.empr.com/home/news/single-dose-solosec-approved-for-trichomoniasis/?utm_source=newsletter&utm_medium=email&utm_campaign=mpr-dailydose-hay-20210718&cpn=&hmSubId=T4560dVaSjY1&hmEmail=slhn2hv2DuT0G107edAyLI_fndfC6gq0&NID=1346274941&c_id=&email_hash=c39006794671 6c8790557377ce89c71c&dl=0&mpweb=1323-142847-1047198 accessed 07-17-2021

89

Spinosad (Natroba)

- Topical suspension
- Pediculocide
- Approved for the treatment of scabies in patients 4 years of age and older
- Adverse events:
  - 1% application site irritation and dry skin
- Also indicated for head lice in individuals 6 months of age and older

90

Hexavalent Pediatric Vaccine Approved

- Vaxelis:
  - diphtheria and tetanus toxoids and acellular pertussis adsorbed, inactivated poliovirus, haemophilus b conjugate [meningococcal protein conjugate] and hepatitis B [recombinant] vaccine
    - Active immunization in children aged 6 weeks through 4 years (prior to the 5th birthday)
    - 3-dose series given at 2, 4, and 6 months of age
  - It may be used to complete the hepatitis B series
  - The 3-dose series does not constitute a primary immunization series against pertussis; an additional dose of pertussis-containing vaccine is needed to complete the primary series

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Thank You!
I Appreciate Your Attention!

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