GUIDANCE FOR ANTIBIOTIC INTERCHANGE DURING AMOXICILLIN SUSPENSION SHORTAGE

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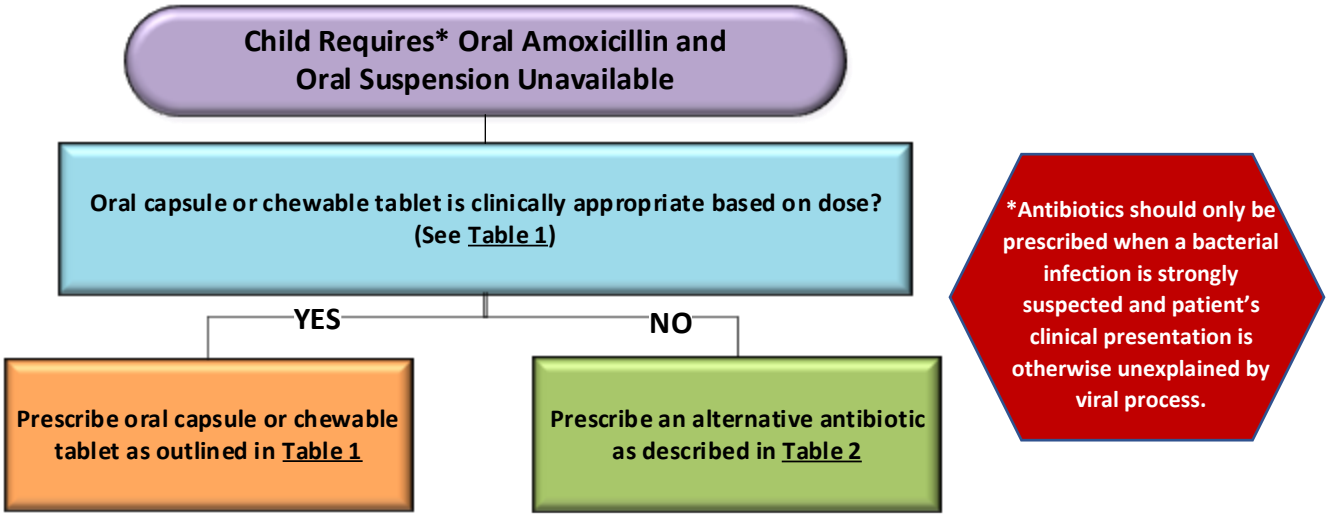
Antibiotic Interchange during Amoxicillin Suspension Shortage



The use of oral cephalosporins, in place of amoxicillin, for treatment of bacterial CAP, AOM, or rhinosinusitis is ***strongly discouraged***. In addition to posing an increased risk for *C. difficile* infection and multi-drug resistance, second and third generation oral cephalosporins have poor oral absorption, decreased lung penetration, and provide inferior coverage of *S. pneumoniae.* See text below for more information.

Table 1: Amoxicillin Capsule and Chewable Tablet Interchange

Amoxicillin Oral Suspension Dose *(Based on 30-45 mg/kg/dose)*	**125 mg Chewable Tablet*** (Quantity of tablets to prescribe per dose)	**250 mg Chewable Tablet*** (Quantity of tablets to prescribe per dose)	**250 mg Capsule^** (Quantity of capsules to prescribe per dose)	**500 mg Capsule^** (Quantity of capsules to prescribe per dose)
50 mg to 70 mg	1/2 tablet	-	-	-
70 mg to 94 mg	-	-	-	-
95 mg to 149 mg	1 tablet	1/2 tablet	-	-
150 mg to 199 mg	1 and 1/2 tablets	-	-	-
200 mg to 299 mg	2 tablets	1 tablet	1 capsule	-
300 mg to 399 mg	3 tablets	1 and 1/2 tablets	-	-
400 mg to 574 mg	-	2 tablets	2 capsules	1 capsule
575 mg to 849 mg	-	3 tablets	3 capsules	-
850 mg to 1,100 mg	-	4 tablets	4 capsules	2 capsules

Capsule Administration

Feeding tube: open capsule into 15-30 mL of water and administer per tube. Flush with 10 mL of water

Oral: Open capsule into juice, apple sauce, or pudding and consume immediately

capsules should only be used for whole capsule dosing

*Chewable tablets (125 mg and 250 mg) may be split

^Capsules (250 mg and 500 mg) should only be used for whole capsule dosing

Table 2: Alternative Agent Interchange

Disease State	Alternative Agent(s) and Recommended Dosing *Unless specified, suggested dosing is for patients >1 month of age with normal renal function*	Duration of Therapy[4, 10-12]
Acute Otitis Media	**PO Amoxicillin/clavulanate (PREFERRED)** <1 month: 15 mg/kg/dose of amoxicillin component BID ≥1 month: 45 mg/kg/dose of amoxicillin component BID[a] (max: 4 g/DAY amoxicillin) **IM Ceftriaxone x 1 dose** 50 mg/kg/dose IM x 1 dose (max dose: 500 mg) **PO Cefuroxime** *(if penicillin allergic but able to tolerate cephalosporin)* 15 mg/kg/dose BID (max: 500 mg/dose) **PO Clindamycin#** 13 mg/kg/dose TID (max: 450 mg/dose)	Oral regimen: <2 years: **10 days** ≥2 years: **5 days** IM Ceftriaxone: **Single dose**
Community Acquired Pneumonia	**PO Amoxicillin/clavulanate (PREFERRED)** 30 mg/kg/dose of amoxicillin component TID[a,b,c] (max: 4 g/DAY amoxicillin) **PO Clindamycin** 13 mg/kg/dose TID (max: 450 mg/dose) **PO Doxycycline** 2.2 mg/kg/dose BID (max: 100 mg/dose)	**5 days**
Acute Bacterial Sinusitis	**PO Amoxicillin/clavulanate (PREFERRED)** 30 mg/kg/dose of amoxicillin component TID[a,b,c] (max: 4 g/DAY amoxicillin) **PO Doxycycline** 2.2 mg/kg/dose BID (max: 100 mg/dose)	**5 days**
Group A *Streptococcus* Pharyngitis	**PO Penicillin VK (PREFERRED)** <27 kg: 250 mg PO BID-TID ≥27 kg: 500 mg PO BID-TID **IM Penicillin G Benzathine (PREFERRED)** <27 kg: 600,000 units IM x 1 dose ≥27 kg: 1.2 million units IM x 1 dose **PO Cephalexin** (*if penicillin allergic but able to tolerate cephalosporin*) 20 mg/kg/dose PO BID (max: 500 mg/dose)	Oral regimen: **10 days** IM Penicillin G: **Single dose**
Asplenia Prophylaxis	**PO Penicillin VK** < 3 years: 125 mg BID ≥3 years: 250 mg BID	-
UTI *Prophylaxis*	**PO Trimethoprim/Sulfamethoxazole** 2-3 mg/kg/dose trimethoprim component once daily (max: 160 mg/dose) **PO Nitrofurantoin** 1-2 mg/kg/dose once daily (max: 100 mg/dose)	-
UTI Treatment (Cystitis)	**PO Nitrofurantoin (PREFERRED)** *(NOT for pyelonephritis or upper UTI)* ≥2 months: MacroDANTIN 1.75 mg/kg/dose QID (max: 100 mg/dose) ≥12 years: MacroBID 100 mg BID **PO Cephalexin** 12.5 mg/kg/dose PO QID (max: 500 mg/dose) **PO Cefadroxil** 15 mg/kg/dose BID (max: 1 g/dose)	**3-5 days**
UTI Treatment (Pyelonephritis)	**PO Cephalexin (PREFERRED)** 25 mg/kg/dose PO QID (max: 1 g/dose) **PO Cefadroxil** 15 mg/kg/dose BID (max: 1 g/dose)	**7-10 days**

a: Amoxicillin/clavulanate ES 600 mg/42.9 mg/5 mL is the preferred formulation for children ≥1 month of age. **b:** The pharmacodynamics of amoxicillin are best optimized when the total daily dose is divided at least three times daily for treatment of infections outside of the middle ear. The recommendation to use twice daily dosing of amoxicillin is based on a pharmacokinetic study which documented the half-life of amoxicillin in middle ear fluid to be 4–6 hours, compared with a half-life of 1 hour in serum. Similar data supporting BID dosing of amoxicillin for pneumonia are not available. To the contrary, Bradley et al. demonstrated clinical and microbiologic cure in 90% of patients receiving high-dose amoxicillin (90 mg/kg/day) divided TID versus *only 65%* when divided BID for treatment of susceptible *S. pneumoniae* pneumonia with penicillin MIC of 2 mcg/mL.[9] **c**: If ≥40 kg and able to swallow tablets, may use amoxicillin/clavulanate XR 2,000 mg BID (usually requires prior authorization). **d**: Of note, original data describing enamel staining are from studies with tetracycline. Recent comparative data in children suggest that doxycycline is NOT likely to cause visible teeth staining or enamel hypoplasia in children. **The American Academy of Pediatrics recommend that doxycycline can be administered in any pediatric patient for durations ≤21 days without regard to the patient's age**.[4] **#**: Clindamycin does not provide coverage of Gram-negative respiratory pathogens, including *H. influenzae*.

RATIONALE FOR AGENT SELECTION AND DOSING (CAP, AOM, BACTERIAL RHINOSITIS):

Oral amoxicillin is the drug of choice for treatment of community acquired pneumonia. Oral third generation cephalosporins are often inappropriately prescribed for treatment of CAP.[5] The knowledge that IV ceftriaxone provides excellent coverage of *S. pneumoniae* often creates the misconception that all third generation cephalosporins provide coverage equivalent to amoxicillin. Rather, the contrary is true as oral third generation cephalosporins have poor oral absorption, decreased lung penetration, and provide inferior coverage of *S. pneumoniae* (greater than 60% of Serotype 19A pneumococci are resistant to oral cephalosporins).[6-8] No oral cephalosporin provides activity against *S. pneumoniae* at the site of infection that equals high-dose amoxicillin.[2] Lastly, the pharmacokinetics of amoxicillin are best optimized when the total daily dose is divided at least three times daily. The recommendation to use twice daily dosing of amoxicillin is based on pharmacokinetic studies which documented the half-life of amoxicillin in middle ear fluid to be 4–6 hours, compared with a half-life of 1 hour in serum. Similar data supporting a recommendation for twice daily dosing of amoxicillin have not been collected for documented pneumococcal pneumonia in children. To the contrary, Bradley et al. demonstrated clinical and microbiologic cure in 90% of patients receiving high-dose amoxicillin (90 mg/kg/day) divided three times daily versus *only 65%* when divided twice daily for treatment of susceptible *S. pneumoniae* pneumonia with penicillin MICs of 2 mcg/mL.[(9)]

RATIONALE FOR AGENT SELECTION AND DOSING (UTI):

Oral first generation cephalosporins and nitrofurantoin* are the preferred empiric agents for treatment of UTIs in pediatric patients. Per CLSI laboratory standards, **cefazolin** serves as the surrogate to determine susceptibility for **ALL** oral cephalosporins for treatment of *E. coli, K. pneumoniae,* and *P. mirabilis* isolated from the urine. As such, rates of susceptibility for such uropathogens are identical for oral third (ie cefdinir, cefuroxime, cefixime) and first generation (ie cephalexin, cefadroxil) cephalosporins. The empiric use of third generation cephalosporins for treatment of UTIs in pediatric patients is strongly discouraged as their use contributes significantly to the development of Gram-negative resistance, including ESBL-production. Cefdinir has poor urinary penetration (<15% in pediatrics) and is NOT recommended as an alternative agent within the AAP UTI Guidelines.

**NOTE: nitrofurantoin should not be used for treatment of upper UTIs or pyelonephritis*

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