

Clinical practice guidelines for acute otitis media in children: A systematic review and appraisal of European national guidelines

Supplementary File 8: Antibiotic treatment recommended by European, American and WHO guidelines for acute otitis media (AOM) in children

Guideline	First line*	Duration of first line therapy	Second line/Treatment failure	Third line/ Allergy to first line	National LOE / SOR	Oxford LOE /SOR
Belgium	PO amoxicillin 75mg-100/kg/day in 3 divided doses	7 days	<u>Treatment failure</u> : cefuroxime axetil 30-50 mg / kg in 3 doses amoxicillin-clavulanic acid 50 / 37.5 mg / kg in 3 doses	<u>In case of Allergy to cephalosporins</u> , either: Co-trimoxazole (Trimethoprim 8 mg/kg/day and Sulfamethoxazole 40 mg/kg/day) in 3 divided doses Levofloxacin 10 mg/ kg/day in 2 divided doses	For treatment choice: Expert Opinion/Weak recommendation Duration: GRADE A - B, low recommendation)	For treatment choice: 5 /X For duration: 1a-1b/ X
Czech Republic	PO amoxicillin 75-90mg/kg/day in 3 divided doses	7-10 days	Discusses targeted therapy to specific bacterial agents, but no empiric antibiotic for treatment failure	<u>Allergy to beta lactams:</u> co-trimoxazole	None	None
Denmark	PO Penicillin V 60mg/kg/day in 3 divided doses	7 days	<u>Treatment failure</u> <u><2 years of age:</u> Amoxicillin-clavulanic acid	<u>Penicillin allergy:</u> clarithromycin 7.5mg.kg/dose x2 for 7 days	Level 1a-1c and 5 / Grade A and √	Level 1a-1c and 5

			10/2.5mg/kg/dose 8 hourly for 7 days <u>2-12 years of age:</u> amoxicillin – clavulanic acid 1- /2.5mg/kg/dose 8 hourly for 7 days		For duration: No LOE/SOR	
Finland	PO Amoxicillin 40mg/kg/day 8-12 hourly OR PO amoxicillin-clavulanic acid 40/5.7mg/kg/day in 2-3 divided doses	5 -7 days	<u>If vomiting:</u> IM Ceftriaxone (one dose)	<u>Penicillin allergy:</u> cefaclor, cefuroximexetil, sulfa trimethoprim, azithromycin or clarithromycin	First line: C / C (None for treatment duration)	1b, 2b-2c, and 3b-4
France	PO amoxicillin 80-90mg/kg/day in 2-3 divided doses	5 day duration if >2 years of age, 8-10 days if <2 years of age	<u>Treatment failure:</u> PO Amoxicillin/clavulanic acid 80mg/kg/day) AND PO amoxicillin 70mg/kg/day) OR IM/IV ceftriaxone 50mg/kg daily for 3 days PO Amoxicillin/clavulanic acid = otitis conjunctivitis syndrome	Allergy to beta lactams erythromycin-sulfafuraole or cotrimoxazole Allergy to penicillins without allergy to cephalosporins: cefpodoxime	Only duration has LOE: Level 1 and Professional Agreement/ Grade A Duration for child <2 years of age is Level 1/ Grade A >2 years of age is professional agreement (No LOE) 3 rd line treatment: Professional agreement (No LOE)	Level 1a

Germany	<p>PO Amoxicillin 50mg/kg/day in 2-3 divided doses</p> <p><u>If from country with high rates of penicillin resistance:</u> PO amoxicillin 80-90mg/kg/day</p>	7 days	<p><u>Treatment failure:</u> PO amoxicillin 80-90mg/kg/day</p> <p>Second choice: PO cephalosporin including cefuroxime axetil (20-30mg/kg/day for 5 days),</p>	<u>Allergy to penicillins/cephalosporins:</u> macrolide ie erythromycin 7 days	None	None
Ireland	Amoxicillin (no duration, no route, no frequency)	None	None	None	None	None
Italy	<p><u>Mild symptoms and no otorrhea nor risk factors† :</u> PO Amoxicillin 50mg/kg/day in 2-3 divided doses</p> <p><u>Severe symptoms, otorrhea, or risk factors for bacterial resistance</u> Amoxicillin-clavulanic acid 80-90mg/kg/day in 2-3 divided doses</p>	<p>Duration:</p> <p>10 days <2 years of age 5 days >2 years of age</p>	<p><u>Treatment failure:</u> <u>If they were treated with amoxicillin or cefaclor:</u> amoxicillin plus clavulanic acid or cefpodoxime proxetil or cefuroxime axetil.</p> <p><u>If they were being treated with a broad-spectrum antibiotic:</u> intramuscular or intravenous ceftriaxone 50mg/kg once daily</p> <p>Duration: 10 days <2 years of age or spontaneous otorrhea 5 days >2 years of age 3 days for ceftriaxone</p>	<u>Penicillin allergy:</u> macrolide	<p>First line (for both) : Level I/ Grade A</p> <p>Treatment failure: Level II/ Grade B</p> <p>Duration Level I/ Grade B</p> <p>Allergy: VI/D</p>	<p>First line: Level 1a- 1b/ A</p> <p>Treatment failure: Level 1b/ X</p> <p>Duration: Level 1a-1b /X</p>

Luxembourg	Amoxicillin 80-90mg /kg/day in 3 divided doses <u>Alternatively if 'very severe cases'</u> Amoxicillin-clavulanic acid 80-90mg/kg/day in 3 divided doses	<6 years of age 10 days treatment >6 years 5-7 days treatment	<u>Treatment failure:</u> Amoxicillin/clavulanate Otherwise cefuroxime axetil (no dose, no frequency) or ceftriaxone 50mg/kg/day for 3 days or azithromycin or clarithromycin or clindamycin	<u>If vomiting:</u> Ceftriaxone 50 mg / kg once daily for 3 days <u>Penicillin allergy:</u> Cefuroxime 30mg/kg in two divided doses <u>Allergy to penicillin + cephalosporin:</u> Azithromycin 10mg/kg/day for 6 days or clarithromycin 15mg/kg/day in two divided doses Otherwise: sulfamethoxazole-trimethoprim 60/19mg/kg of trimethoprim per day or clindamycin 30-40mg/kg in three divided doses	Not applicable	None Not applicable
Netherlands	Amoxicillin 40mg/kg/day in 3 divided doses	7 days	<u>Second line and also treatment failure:</u> Amoxicillin-clavulanic acid 40/10mg/kg/day in 3 divided doses for 7 days	<u>Penicillin allergy:</u> cotrimoxazole 36mg/kg/day in two divided doses; 5-7 days	Not applicable	Not applicable
Norway	PO phenoxymethylpenicillin 24-60mg/kg/day in 3-4 divided doses per day <u>In case of frequent/recurrent cases:</u>	5 days	<u>Treatment failure:</u> trimethoprim sulfamethoxazole (for children)	<u>Allergy:</u> <25kg: Erythromycin oral solution (ethyl succinate) 40mg/kg/day in two divided doses for 5 days or Clarithromycin (children over 6 months) 15 mg/kg/day in two divided doses for 5 days	None	None

	Amoxicillin 21-42mg/kg/day in three divided doses			25-35kg: Erythromycin enteric capsules 500mg/kg/day in two divided doses for 5 days or Clarithromycin 14 mg/kg/day in two divided doses for 5 days		
Poland	PO amoxicillin <40kg: 75-90mg/kg/day in 2 divided doses >40kg 3000-4000mg per day in 2 divided doses	If <2 years of age, 10 days duration If >2 years of age, 5 days duration	<u>Treatment failure:</u> Amoxicillin/clavulanic acid <40kg: 70-90mg/kg/day in two divided doses >40kg: 3000mg-4000mg per day in 2 divided doses IVceftriaxone <40kg 50mg/kg/day once daily for 3 days >40kg 1-2g/day once daily for 3 days	<u>Allergy to amoxicillin:</u> PO Cefuroxime axetil >40kg 1000mg/day in 2 divided doses for 5 days <40kg 30mg/kg/day in two divided doses for 5 days unless if <2 yoa then for 10 days <u>Allergy to amoxicillin and severe infection:</u> Ceftriaxone >40kg- 1-2g IV/IM per day once daily for 3 days <40kg- 50mg/kg IV/IM per day once daily for 3 days Allergy to beta lactams: Clarithromycin <40kg 15-20mg/kg/day in two divided doses; >40kg 500-1000mg/day in two divided doses	First line: Level II /Grade A First line duration: Level II /Grade B Treatment failure: Level II-III/ Grade A-B Allergy treatment: Level I-II/ Grade A-B	First line antibiotic: Level 2a and 3a First line duration: Level 2a and 3a Treatment failure: Level 2a, 3a, 4, and 5 Allergy treatment: 1a, 2a, 3a

Portugal	Amoxicillin 80-90mg/day in 2 divided doses	5 days routine or <2 years of age 7 days if <2 years, recurrent, failure of initial treatment 10 days if recurrent AOM	<u>Treatment failure:</u> PO/IV Amoxicillin and clavulanic acid 80-90mg/kg/day in 2 divided doses or PO Cefuroxime-axetil 30mg/kg/day in 2 divided doses or IV 80-100mg/kg/day in 3 divided doses 7 days if <2 years OR IM/IV Ceftriaxone 50mg/kg/day once daily	<u>Penicillin allergy:</u> Clarithromycin 50mg/kg/day in 2 divided doses or Erythromycin 50mg/kg/day in 3-4 divided doses per day or Azithromycin 10mg/kg/day once a day	First line: Level A/ Grade 1 Treatment failure: Level B/ Grade IIa Duration: 7 days- Level A / Grade IIa 5 days- Level A/ Grade 1 10 days no evidence Allergic treatment: Level C/Grade I	First line: level 1a, 2a, or 3a Treatment failure: Level 1b, 2b, or 3b Duration: 7 days- level 1a, 2a, or 3a 5 days- level 1a, 2a, or 3a 10 days no evidence Allergic treatment Level 4-5 s
Spain	PO Amoxicillin 80-90mg/kg/day in 3 divided doses <u>If <6 months, severe symptoms, family history of ENT complications, previous therapeutic failure</u> Amoxicillin/clavulanic acid 80-90mg/kg/day in 3 divided doses for 7-10 days <u>If <2 months of age:</u>	Routine: 5 days Otherwise: 10 days	<u>Treatment failure:</u> Amoxicillin-clavulanic acid 80-90mg/kg/day in 3 divided doses for 7-10 days or IM/IV Ceftriaxone 50mg/kg/day for 3 days	<u>Penicillin allergy:</u> Cefuroxime axetil 30mg/kg/day in 2 divided doses <u>If anaphylaxis to penicillin:</u> Clarithromycin 15mg/kg/day in 2 divided doses for 7 days or azithromycin 10mg/kg once daily on first day, then 5mg/kg once daily for 4 additional days. Can also give Levofloxacin 6 months-5 yoa: 10mg/kg every twelve hours >5 yoa give 10mg/kg every 24 hours	First line: Level II/ Grade B For children requiring amoxicillin-clavulanic acid as first line: Level II/ Grade B (No evidence for <2 months of age) Treatment failure: Level III/Grade C; for	First line: 2a For children requiring amoxicillin-clavulanic acid as first line: Level 2a-3a Treatment failure: Level 4-5 ; Ceftriaxone as used in treatment failure: Level 1a

	IV cefotaxime or PO/ IV amoxicillin-clavulanic acid. For PO only if no fever or no symptoms. No LOE				ceftriaxone Level I/Grade A Allergic to penicillin/cephalosporin: Level III/Grade C	Allergy to penicillin/cephalosporin: Level 4-5
Sweden	PO Penicillin V 75 mg / kg/day in 3 divided doses <u>If recurrent: (new acute otitis media within a month with symptom-free intervals):</u> Penicillin V 75mg / kg/day in 3 divided doses or Amoxicillin 60 mg / kg/day in 3 divided doses	Routine: 5 days Recurrent: 10 days	<u>Treatment failure:</u> Amoxicillin 60mg/kg/day in 3 divided doses for ten days.	<u>Penicillin allergy:</u> Erythromycin 40mg/kg/day in 4 divided doses or 40mg/kg/day in 2 divided doses	Not applicable	Not applicable
Switzerland	Amoxicillin 50mg/kg/day in 2 divided doses <u>If risk factors or from country with high rates of penicillin resistance:</u> Amoxicillin 80mg/kg/day in 2 divided doses	Routine: 5 days <2 years of age, previous otitis media, perforated tympanic membrane or from country with high rates of penicillin resistance : 10 days	‡Amoxicillin/clavulanic acid 80mg/kg/day in two divided doses for 10 days ‡ or Ceftriaxone 50mg/kg daily for 1-3 days	None	Not applicable	Not applicable
UK SIGN (refers to BNF for Children)	Amoxicillin	5-7 days	<u>Treatment failure:</u> Amoxicillin-clavulanic acid	<u>Penicillin allergy:</u>	None	None

	<p>Child 1-11 months of age: 125mg three times a day for 5-7 days</p> <p>Child 1-4 years: 250mg three times a day for 5-7 days</p> <p>(NB: dosage can be both low and high dose amoxicillin dependently on kg; for example If 1 yoa and weight <50th centile, will be given high dose; if 2 yoa and weight at 50th centile, would be given low dose.</p>		(dose dependent on suspension available)	Clarithromycin or erythromycin ; dosage dependent on age		
USA	<p>Amoxicillin (80–90 mg/ kg/ day in 2 divided doses</p> <p>OR</p> <p>If amoxicillin past 30 days, concurrent purulent conjunctivitis (otitis conjunctivitis syndrome), or history of AOM non responsive to amoxicillin:</p> <p>Amoxicillin-clavulanic acid (90 mg/kg/ day amoxicillin dosage in 2 divided doses</p>	<p><2 years of age: 10 days</p> <p>2-5 years of age:7 days</p> <p>>6 years of age 5-7 days</p>	<p><u>Treatment failure:</u></p> <p>Amoxicillin-clavulanic acid 90mg/kg/day 12 hourly</p> <p><2 years of age: 10 day course</p> <p>2-5 years of age 7 day course</p> <p>>6 years of age 5-7 days</p> <p>OR</p> <p>IM/IV Ceftriaxone 50mg daily 3 days</p>	<p><u>Penicillin allergy:</u></p> <p>Cefdinir 14mg/kg per day in 1-2 divided doses or cefuroxime 30mg/kg per day in 2 divided doses or cefpodoxime 10mg/kg per day in 2 divided doses or ceftriaxone 50mg IM or IV per day for 1-3 days</p>	<p>First line : B, recommendati on; first line amoxil-clav: C, recommendati on</p> <p>Treatment failure: B, recommendati on</p>	<p>First line: 2a or 3a</p> <p>First line amoxi clav: 2a, 3a, 4</p> <p>Treatment failure: 2a, 3a</p>

WHO	PO amoxicillin 80mg/kg/day in 2 divided doses If consider pathogen sensitive, give co- trimaxazole, dose: (trimethoprim component 8mg/kg/day 12 hourly for 5 days)	7-10 days	Repeat antibiotics for another 5 days	None	Low quality evidence/ Strong recommenda tion	Level 4
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NB Amoxicillin-clavulanic acid dose always given in terms of amoxicillin component dosage.

* Routinely to treat with low-dose amoxicillin, but for high dose amoxicillin in the following situations: Switzerland: If from area of high penicillin resistance, age <6 months, severe symptoms. UK: "If necessary." Germany: area of high penicillin resistance

† Italy risk factors: risk factors for bacterial resistance: age <3 years, day-care attendance, older siblings, recent antibiotic therapy (<1 month), no PCV-7.

‡ Switzerland: If <6 months, severe symptoms, family history of ENT complications, previous therapeutic failure, recent administration of amoxicillin, concurrent purulent conjunctivitis or otorrhoea , region of high penicillin resistance or risk factors for antibiotic resistant for PO amoxicillin-clavulanic acid as first line.