

Amoxycrav - MCC Standardised Package Insert vs Originator and International References

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	Standard	Augmentin	USPD	UK Augme	Canada (Apo TGA (Augmentin Duo)
1. INDICATIONS					
Upper respiratory tract infections (caused by amoxycillin-resistant organisms producing beta-lactamases sensitive to clavulanic acid) eg sinusitis, recurrent otitis media, tonsillitis	x	x	N, not tonsil	x	N, URTI beta- x
Lower respiratory tract infections (caused by amoxycillin-resistant organisms producing beta-lactamases sensitive to clavulanic acid): eg bronchitis, bronchopneumonia	x	x	x	x	N, beta-lacta x
Genito-urinary tract infections (caused by amoxycillin-resistant organisms producing beta-lactamases sensitive to clavulanic acid) eg cystitis, urethritis, pyelonephritis	x	x	x	x	N, UTI beta-l x
Skin and soft tissue infections (caused by amoxycillin-resistant organisms producing beta-lactamases sensitive to clavulanic acid)	x	x	x	x	N, SSTI beta- x
Infections caused by amoxycillin-sensitive organisms at the appropriate amoxycillin dosage	x	x	N	N	x
Total	5	5	3	4	1
p= proportion		p=5/5=1.00	p=3/5=0.60	p=4/5=0.80	p=1/5=0.20
2. RECOMMENDED DOSAGE					
Dosage					
Tablets to be taken immediately before a meal	x	x	N, full or em	x	N, full or em x
Infections caused by amoxycillin-sensitive organisms use the approved amoxycillin dosage	x	x	N	x	N
Adults: 1 x 375 mg q8h at start of meal.	x	N. 1-2 x 37 N, 375 mg	x	N. 375 mg q8 N. 625 mg q12h	N. 1000 mg q N. 1000 mg q12h
For more severe infections & infections of respiratory tract 1 x 675 mg q8h at start of meal	x	x	x	x	N. 1000 mg q N. 1000 mg q12h
All tablet strengths contain 125mg clavulanic acid; 2 x 375 mg tablets# 1 x 675 mg tablet and should not be substituted	x	x	x	x	x
Amoxycillin-sensitive organisms: URTI, UTI, Skin & Soft Tissue : 1 x 375 mg q8h.	x	N. 1-2 x 37 N, according	N	N	N
Amoxycillin-sensitive organisms: URTI, LRTI, UTI, Skin & Soft Tissue : 1 x 625 mg q8h.	x	x	N, according	N	N
Amoxycillin-sensitive organisms: URTI, LRTI, UTI, Skin & Soft Tissue : 1 x 1000 mg q12h.	x	x	N, according	N	N
Amoxycillin-resistant organisms: UTI, Skin & Soft Tissue : 1 x 375 mg q8h.	x	N. 1-2 x 37 N, according	N	N	N
Amoxycillin-resistant organisms: URTI, LRTI, UTI, Skin & Soft Tissue : 1 x 625 mg q8h.	x	x	N, according	N	N
Amoxycillin-resistant organisms: URTI, LRTI, UTI, Skin & Soft Tissue : 1 x 1000 mg q12h.	x	x	N, according	N	N
Impaired renal function: Dose may need to be reduced or interval extended	x	x	N	N	x
Mild (Cr Cl > 30 ml/min) - no change	x	x	x	x	x
Moderate (Cr Cl 10 - 30 ml/min) - 1 tablet q12h	x	x	x	N	x
(Severe (Cr Cl< 10 ml/min) - half tablet q12h	x	x	N, q12h	N, 375 mg (N	N, 625 mg Q24h
Haemodialysis decreases serum concentrations. Additional dose necessary at end of dialysis	x	N	x	N	x
Total	16	12	5	7	2
p= proportion		P=12/16=0	P=5/15=0.31	p=7/16=0.4	p=2/16=0.13
3. CAUTIONS					
Warnings					
Warnings					
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions	x	x	x	x	x
Before initiating therapy, careful enquiry about previous hypersensitivity reactions to penicillins, cephalosporins or other allergens shd be made	x	x	x	N	x
If allergic reaction occurs, discontinue & institute appropriate therapy, eg adrenaline, oxygen, iv steroids, airway management	x	x	x	N	x
Avoid if infectious mononucleosis is suspected due to morbilliform rash associated with amoxycillin	x	N	x	x	x
Overgrowth of non-susceptible organisms with prolonged use	x	N	x	x	x
Pseudomembranous enterocolitis	x	N	x	N	x
Prolongation of prothrombin time - appropriate monitoring in patients receiving anticoagulants	x	N	N	N	N
Periodic assessment of organ function, including renal, hepatic and haemopoietic function advisable in prolonged therapy	x	x	x	N	x
Transient hepatitis & cholestatic jaundice - use with caution in hepatic dysfunction	x	x	x	x	x
Total	9	5	8	4	7
Pregnancy & Lactation					
Safety in pregnancy not established	x	x	x	x	x
Amoxycillin distributed in breast milk, may lead to sensitisation, diarrhoea, candidiasis and skin rash in the infant	x	N	x	sensitisation on only	N, no consequences
Contra-indications					
Hypersensitivity to penicillins or cephalosporins due to documented cross-sensitivity	x	x	x	x	x
Previous history of amoxycillin/clavulanic-associated jaundice/hepatic dysfunction	x	x	x	x	x
Total	4	3	4	3	3

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Special precautions

Jarisch-Herxheimer reaction when administered to patients with syphilis	x	N	N	N	N	N	
Adequate fluid intake and urinary output must be maintained with high doses	x	N	N	x	N	N	
Sodium content (esp in high doses) to be considered in pts on sodium-restricted diets	x	N	N	N	N	N	
Lignocaine or benzyl alcohol to be used im not iv	x	N	N	N	N	N	
Periodic assessments of organ system functions incl renal, hepatic and haemopoietic function advised during prolonged therapy	x	x	x	N	x	x	
Not treatment of choice in sore throat/pharyngitis due to possibility of infectious mononucleosis	x	x	N	x	N	x	
Use with caution in lymphatic leukaemia due to susceptibility to amoxycillin-induced skin rashes	x	x	N	N	N	x	
Superinfections with mycotic or bacterial pathogens (usually Aerobacter, Pseudomonas or Candida)	x	x	N	N	x	x	
Changes in liver function - use with caution in pts with severe hepatic dysfunction	x	x	x	x	x	x	
Dosage adjustment in moderate or severe renal impairment	x	x	x	x	x	x	
Amoxycillin is excreted in human milk - use with caution in nursing women	x	x	x	N	x	x	
Use may lead to selection of resistant strains - therefore perform sensitivity testing if possible	x	N	x	N	x	x	
Total	12	7	5	4	6	8	
p= proportion							

Mean of p values=Overall p value 0.60+0.68+0.44+0.64+0.76+5=0.62
 $q=1-0.62=0.38$
 $pq=0.427 \times 0.573=0.24$
Std Deviation= $\sqrt{(pq \times n)} = \sqrt{(0.24 \times 5)} = \sqrt{0.05}=0.22$
95% CI = $p \pm (2.776 \times \text{Std Dev}) = p \pm (2.776 \times 0.22) = p \pm 0.61$
95%CI = 0.62±0.61 ie. 1.23 to 0.01

Total Cautions

p= proportion	25	15	17	11	16	19	
		p=15/25=0.6	p=17/25=0.68	p=11/25=0.44	p=16/25=0.64	p=19/25=0.76	

4. SIDE EFFECTS

Most frequent: diarrhoea, nausea, vomiting, indigestion, abdominal pain, skin rashes, urticaria, erythema multiforme, vaginitis, abnormal taste, headache, dizziness, tiredness, hot flushes	x	x	N	N	N	N	
Minimise adverse effects esp. nausea & diarrhoea by taking at start of meal	x	x	N	x	x	x	
Clavulanate causes GIT symptoms, so if higher concentration of amoxycillin is required, additional amoxycillin should be given separately	x	x	N	N	N	N	
Skin rashes	x	x	x	x	x	x	
Pruritus	x	x	x	N	x	x	
Urticaria	x	x	N	x	x	x	
Serum-sickness-like syndrome	x	x	x	x	x	x	
Erythema multiforme	x	x	x	x	x	x	
Stevens-Johnson syndrome	x	x	x	x	x	x	
Hypersensitivity vasculitis	x	x	N	x	x	x	
Bullous exfoliative dermatitis	x	x	N	x	x	x	
Toxic epidermal necrolysis	x	x	N	x	x	x	
Serious and occasional fatal hypersensitivity (anaphylactic) reactions and angioneurotic oedema	x	x	x	x	x	x	
Interstitial nephritis	x	x	N	x	x	x	
Nausea	x	x	x	x	x	x	
Vomiting	x	x	x	x	x	x	
Diarrhoea	x	x	x	x	x	x	
Gastritis	x	x	x	N	N	x	
Stomatitis	x	x	N	N	x	x	
Glossitis	x	x	x	N	x	x	
Black "hairy" tongue	x	x	N	N	x	x	
Enterocolitis	x	x	N	N	x	x	
Mucocutaneous candidiasis	x	x	x	N	x	x	
Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis)	x	x	x	x	x	x	
Hepatitis	x	x	N	x	x	x	
Cholestatic jaundice, usually reversible, but death is extremely rare, associated with serious underlying disease or concomitant medication	x	x	x	x	x	x	
Rise in AST and/or ALT	x	x	x	x	x	x	
Crystalluria	x	N	N	x	N	N	
Haemolytic anaemia	x	x	N	x	x	N	
Reversible thrombocytopenia	x	x	N	x	x	x	
Thrombocytopenic purpura	x	x	N	N	x	x	
Eosinophilia	x	x	N	N	x	x	
Reversible leucopenia	x	x	x	x	x	x	
Agranulocytosis	x	x	N	x	x	x	
Slight thrombocytosis	x	x	N	N	x	x	
Prolongation of bleeding time and prothrombin time	x	x	x	x	x	x	
Reversible hyperactivity	x	x	N	x	N	x	
Dizziness	x	x	N	x	x	x	
Headache	x	x	x	x	x	x	
Convulsions	x	x	x	x	x	x	
Superficial tooth discolouration	x	x	N	x	x	x	
Total	41	40	19	29	36	37	
p= proportion		P=40/41=0.976	p=19/41=0.463	p=29/41=0.707	p=36/41=0.878	p=37/41=0.902	

Mean of p values=Overall p value 0.98+0.46+0.71+0.88+0.90+5=0.79
 $q=1-0.79=0.21$
 $pq=0.79 \times 0.21=0.17$
Std Deviation= $\sqrt{(pq \times n)} = \sqrt{(0.17 \times 5)} = \sqrt{0.03}=0.18$
95% CI = $p \pm (2.776 \times \text{Std Dev}) = p \pm (2.776 \times 0.18) = p \pm 0.47$
95%CI = 0.79±0.47 ie. 1.26 to 0.32

5. DRUG INTERACTIONS

Probenecid - increased and prolonged blood levels of amoxycillin but not clavulanic acid	x	x	x	N	x	x	
							Mean of p values=Overall p value 0.60+1.0+0.40+0.40+0.80+5=0.64

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Reduced efficacy of oral contraceptives - warn patients accordingly	x	x	x	x	x	x	q=1-0.64=0.36
Allopurinol - increased incidence of skin rashes	x	x	x	x	N	x	pq=0.64x0.36=0.23
Tetracyclines and other bacteriostatic drugs may interfere with amoxycillin bactericidal effects	x	N	x	N	N	N	95% CI = $p \pm (2.776 \times \text{Std Dev}) = p \pm (2.776 \times 0.23) = p \pm 0.64$
False positive urine glucose tests if chemical tests are used - use enzymatic glucose oxidase methods	x	N	x	N	N	x	95%CI = 0.64±0.64 ie. 1.28 to 0.00
Total	5	3	5	2	2	4	
p= proportion		p=3/5=0.60	p=5/5=1.0	p=2/5=0.40	p=2/5=0.40	p=4/5=0.80	