

Augmentin ESTM

Anti-Infective Drugs Advisory Committee

January 30, 2001

NDA 50-755 for Augmentin ES

Product :

- Powder for Oral Suspension
- Contains 14 : 1 ratio of amoxicillin : clavulanate
(currently approved Augmentin suspension is 7 : 1)
- Provides 600 mg amoxicillin per 5 mL of suspension
- Dosage: 90 mg/kg/day amoxicillin
(currently approved dosage: 45 mg/kg/day)

Augmentin ES

Developed in response to :

- Public health concern about increasing prevalence of penicillin-resistant *Streptococcus pneumoniae* (PRSP)
- Reports of concomitant prescribing of Augmentin plus amoxicillin for treatment of acute otitis media (AOM)

Regulatory Guidance on AOM and PRSP

- Draft Guidance for Industry: Acute Otitis Media - Developing Antimicrobial Drugs for Treatment (July 21, 1998)
- Anti-Infective Drugs Advisory Committee (July 29, 1998)
 - Discussed PRSP as a pathogen of concern in AOM
 - Repeat tympanocentesis was viewed as an important feature of study design for assessing efficacy against PRSP

History of this NDA

- We developed a protocol (clinical study 536) to assess AOM due to PRSP
- Protocol was submitted to FDA and its design was discussed prior to study initiation in 1999
- Study 536 used repeat-tympanocentesis to assess the primary endpoint of bacterial eradication on-therapy

Clinical Studies of Acute Otitis Media in NDA 50-755

- **Study 536:** bacteriologic and clinical outcomes with Augmentin ES in 521 patients (enriched for enrollment of patients with AOM due to PRSP)
- **Study 447:** clinical study of Augmentin ES vs Augmentin for AOM - 453 patients

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Proposed Indication :

Augmentin ES™ is indicated in the treatment of infections caused by susceptible strains of the designated organisms in the conditions listed below:

Acute Otitis Media — caused by β -lactamase-producing strains of *H. influenzae* or *M. catarrhalis*, and *S. pneumoniae* (including penicillin-resistant strains, MIC value for penicillin ≥ 2 $\mu\text{g/mL}$, when suspected).

Agenda

PK/PD of Antibiotics in Otitis Media

William Craig, MD

Relevant Endpoint Analysis for Efficacy

Colin Marchant, MD

Augmentin ESTM - Bacteriological & Clinical Efficacy in AOM

Brian Wynne, MD

Role of *Augmentin ESTM* in Treating Acute Otitis Media

George McCracken, MD

