

FDA Advisory Committee

December 14-15, 2006

KETEK[®] (telithromycin)

sanofi-aventis US

Introduction

Mark Moyer, MS

Corporate Regulatory Affairs

Overview: KETEK[®] (telithromycin)

- Telithromycin is first in a new class of antimicrobial agents – the ketolides
 - selected to overcome erythromycin resistance in *Streptococcus pneumoniae* isolates
 - lacks α -L-cladinose at position 3 of the erythronolide A ring, resulting in a 3-keto function
 - binds to 2 sites on bacterial ribosome (vs macrolides)
 - focused spectrum of activity against common and atypical bacterial pathogens that cause respiratory tract infections (RTIs)
 - limited activity against nonrespiratory pathogens

Global Status

- Approved in >90 countries worldwide for the treatment of respiratory tract infections in adults:
 - including EU, Canada, Japan, US
 - EU health authority recently approved 5-year renewal of marketing authorization
- Estimated worldwide exposure of 28 million exposures since first launched in Germany (Oct-01)
- Estimated US exposure of 6 million courses

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Presentation Agenda

Introduction

M. Moyer, MS

Medical Need and Resistance

D. Low, MD, FRCPC

Overview of Approval Activities

H. Edelberg, MD, MPH

Postapproval

Microbiology Surveillance

S. Jenkins, PhD

Clinical Importance of Ery-resistant *S. pneumoniae*

J. Lonks, MD

Clinical Safety

B. Rullo, MD

Adverse Events of Special Interest: Hepatic

Safety Overview

B. Rullo, MD

Expert Review

J. Lewis, MD

Epidemiologic Investigation - PHARMetrics

W. Dai, MD, DrPh

Epidemiologic Investigation - Ingenix

A. Walker, MD, DrPh

Expert Review Epidemiology

J. Jones, MD, PhD

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Presentation Agenda

Adverse Events of Special Interest:

Visual Adverse Events

Exacerbation of Myasthenia Gravis

Syncope/Loss of Consciousness

Overview of Safety Experience

B. Rullo, MD

Expert Review: Visual

R. Kardon, MD

Expert Review: Myasthenia Gravis

D. Sanders, MD

Treatment Options for Respiratory Tract Infections

Role of Telithromycin

Overview and CAP

D. Musher, MD

AECB – Etiology, Outcomes and Antibiotics

S. Sethi, MD

Anti-Bacterials in ABS

B.J. Ferguson, MD

Summary and Conclusions

B. Leroy, MD

Clinical Safety Experts in Attendance

Ophthalmology

Randy Kardon, MD, PhD – University of Iowa Hospital and Clinics

Hepatology

James H. Lewis, MD, FACP, FACG – Georgetown University

Neurology

Donald B. Sanders, MD – Duke University

James F. Howard, Jr, MD – University of North Carolina

Cardiology

Craig Pratt, MD – The Methodist Hospital, Houston, TX

Pathology

Emanuel Rubin, MD – Thomas Jefferson University

Clinical Efficacy Experts in Attendance

Adult

Berrylin J. Ferguson, MD – University of Pittsburgh Medical Center

Paul Iannini, MD – Danbury Hospital

John Lonks, MD – Brown University Medical School

Bradley Marples, MD – University of Texas Southwestern Medical Center

Daniel Musher, MD – Baylor College of Medicine

Sanjay Sethi, MD – SUNY at Buffalo

Pediatric

George McCracken, MD – University of Texas Southwestern Medical Center

Epidemiology Experts in Attendance

Gerald A. Faich, MD, MPH, FISPE – United Biosource Corporation

Judith Jones, MD, PhD – The Degge Group Ltd.

Andrew T. McAfee, MD, MSc – i3 Drug Safety

Robert Nelson, PhD – RCN Associates, Inc

Alexander Walker, MD, DrPH – i3 Drug Safety

Microbiology and Statistics Experts in Attendance

Microbiology

Gary Doern, PhD – University of Iowa

Stephen Jenkins, PhD – Mount Sinai School of Medicine

Donald Low, MD, FRCPC – University of Toronto

Biostatistics

Gary Koch, PhD – University of North Carolina

Ketek[®] (telithromycin)

- Microbiologic surveillance demonstrates ongoing medical need
- Positive benefit-risk across all indications
- Postmarketing safety data have led to labeling modifications and enhanced communications
- Safety signals more definitively evaluated in epidemiologic studies
- Risk management ongoing

CAP Indication

- Efficacy demonstrated
 - versus a broad range of comparators
 - against key common and atypical bacterial pathogens
 - against multidrug-resistant *S. pneumoniae* (MDRSP)
 - in outpatients at risk for complications
 - elderly, bilateral pneumonia, pneumococcal bacteremia
- Safety comparable to other antibiotics for this indication

AECB Indication

- Efficacy demonstrated
 - versus a broad range of comparators
 - against key common bacterial pathogens
 - in at-risk subgroups
 - elderly, risk factors for co-morbidities, airway obstruction
- Safety comparable to other antibiotics for this indication

ABS Indication

- Efficacy demonstrated
 - versus standard antibiotic treatments
 - against key common bacterial pathogens
 - in subgroups of interest
 - severe infection per investigator, documented pathogen at entry, total opacity on sinus x-ray
- Safety comparable to other antibiotics for this indication