These results are supplied for informational purposes only.
Prescribing decisions should be made based on the approved package insert in the country of prescription. Ketek is not indicated in this patient population

Sponsor/Company: sanofi-aventis **Drug substance**: Telithromycin (HMR3647)	**Study Identifier:** NCT00315042 **Study code:** EFC6133

Title of the study:
Multinational, randomized, double blind, double dummy, comparative study to evaluate the efficacy and safety of telithromycin oral suspension, 25 mg/kg once daily for 5 days, versus penicillin V oral solution, 13.3 mg/kg three times daily for 10 days, in children 6 months to less than 13 years of age with Streptococcus pyogenes tonsillitis/pharyngitis

Study center(s): Multicenter study in the US with 43 sites

Study period:
Date first subject/patient enrolled: 12 Mar 2006
Date last subject/patient completed: 15 Aug 2006

Phase of development: Phase 3

Objectives:
Primary objective of this study was to compare the bacteriologic efficacy of 5 days of telithromycin to 10 days of penicillin V in subjects with baseline bacterial throat culture positive for Streptococcus pyogenes and repeat throat culture performed at the posttherapy/test-of-cure visit (Visit 3, Days 13 to 17) (per-protocol population for bacteriologic outcome [PPb]).

Methodology:
Multicenter, randomized, double-blind, double-dummy, comparator-controlled study.

Number of subjects/patients:
Planned: 760; Randomized: 314 (the study was terminated on 20 September 2007 before randomization was completed)
Treated: 305; Evaluated: 304 for efficacy; 305 for safety

Diagnosis and criteria for inclusion:
Patients between 6 months to less than 13 years of age with the following inclusion criteria participated:

- Clinical diagnosis of acute tonsillitis/pharyngitis caused by S. pyogenes based on positive result from a rapid detection throat swab test for Group A streptococcal antigen and submission of a throat swab specimen for bacterial culture, identification, and antibiotic-susceptibility testing
- sore and scratchy throat and/or pain on swallowing (odynophagia) together with at least 2 of the following clinical signs: tonsil and/or pharyngeal erythema and/or exudate, cervical adenopathy, uvular edema, and fever.

Investigational product: Telithromycin 50 mg/mL oral suspension
Dose: 25 mg/kg once daily for 5 days
Administration: Oral

Reference therapy: Penicillin V oral solution
Dose: 13.3 mg/kg 3 times daily, to a maximum of 750 mg/day, for 10 days
Administration: Oral

Placebos for telithromycin and penicillin V:
Dose: Not applicable
Administration: Oral

Duration of treatment:
Telithromycin or matching placebo: 5 days
Penicillin V or matching placebo: 10 days
Duration of observation: 38 to 45 days

Criteria for evaluation:
Efficacy:
The primary efficacy assessment was the bacteriologic outcome at the posttherapy/test-of-cure Visit 3 (Days 13 to 17) in the clinically evaluable per protocol population. A patient was considered to be clinically cured if the pathogen identified at baseline were eradicated.

Safety:
The safety assessment included adverse events reported by patients, their parents/legally authorized representative, or observed by the Investigators, specified adverse events of special interest (cardiac, hepatic, and visual) reported spontaneously or elicited, clinical laboratory parameters, and vital signs.

Statistical methods:
Because this study was terminated after randomization of 314 of the planned 760 patients, consequently, the type II error was not controlled as planned, and only descriptive statistics are generated. Comparison of treatment differences between the subgroups and across sites was also not performed.

Analysis of safety measurements (vital signs, laboratory values and adverse events) was performed on all patients who received at least 1 dose of study medication by treatment taken. Adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA Version 10.1).

Summary:
Because of the early termination of the study and limited data, no definite efficacy conclusions can be drawn.

Three hundred fourteen patients were randomized and 305 (97.1%) were included in the PPb population.

Efficacy results:
The primary efficacy assessment of clinical outcome at posttherapy for the PPb population showed that the clinical cure rate for telithromycin was 93.7% (89 of 95) and for penicillin 74.0% (77 of 104).

The observed cure rates in the PPb and bmITT population were higher in the telithromycin group compared the penicillin group at Visit 3 and Visit 4.

Safety results:
No deaths were reported during the study.

Treatment-emergent adverse events were reported by 32.0% of the patients in the telithromycin group and 37.4% in the penicillin group. The most frequently reported treatment-emergent adverse events in ≥3.0% of the patients were: vomiting (telithromycin 7.3%, penicillin 3.2%), cough (telithromycin 4.7%; penicillin 3.2%), otitis media (penicillin 3.2%) and headache (penicillin 3.9%).

One patient (0.7%) in the telithromycin group reported a serious treatment-emergent adverse event associated with study medication overdose but recovered without any clinical intervention. No other adverse events were reported in this patient.

Treatment-emergent adverse events leading to discontinuation were reported by 6% of the patients in the telithromycin group and 3.2% in the penicillin group. Vomiting was the most frequently reported treatment-emergent adverse event that led to discontinuation in the telithromycin group.

Adverse events of special interest were 1 hepatic event eported in the telithromycin group. The patient had an elevated baseline alanine aminotransferase value which returned to normal after treatment. There were 2 visual events (blurred vision) reported, 1 in each treatment group. In both cases the events resolved without sequelae. There were also 2 reported treatment emergent adverse events of study medication overdose in the penicillin group, not considered serious.

There were no patients with postbaseline alanine aminotransferase or aspartate aminotransferase values >3 ULN or postbaseline bilirubin values >2 ULN.

Issue date: 08-Sep-2008