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Prescribing decisions should be made based on the approved package insert in the country of prescription.

Sponsor/Company: sanofi-aventis **Drug substance**: Telithromycin (HMR3647)	**Study Identifier:** NCT00315549 **Study code:** EFC6134
Title of the study: Multinational, randomized, double blind, comparative study to evaluate the efficacy and safety of telithromycin, 800 mg once daily for 5 days, versus penicillin V, 500 mg three times daily for 10 days, in adolescent and adult subjects equal to or over 13 years of age with Streptococcus pyogenes tonsillitis/pharyngitis.	
Study center(s): Multicenter study in the US with 41 sites	
Study period: Date first subject/patient enrolled: 20-Feb- 2006 Date last subject/patient completed: 01-Sep-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) in the per-protocol population for analysis of bacteriologic outcome (PPb).	
Methodology: Multicenter, randomized, double-blind, comparative, 2-parallel treatment group study	
Number of subjects/patients:	
Planned: 760; Randomized: 233 (the study was terminated on 20 September 2007 before randomization was completed)	
Treated: 232; Evaluated: 232 for efficacy; 232 for safety	
Diagnosis and criteria for inclusion: Patients equal to or over 13 years of age with the following inclusion criteria participated: • Clinical diagnosis of acute tonsillitis/pharyngitis caused by Streptococcus pyogenes based on positive result from a rapid detection test for group A streptococcal antigen • 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: t onsil and/or pharyngeal erythema and/or exudate, cervical adenopathy, uvular edema, and fever.	
Investigational product: Telithromycin 400 mg over-encapsulated oral tablets	
Dose: 800 mg once daily for 5 days	
Administration: Oral	
Reference therapy: Penicillin V 250 mg over-encapsulated oral tablets	
Dose: 500 mg 3 times daily 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 233 (78 adolescents) 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.

Two hundred thirty three (233) subjects were randomized out of the targeted population of 760, and of the 233, 155 subjects were in the PPb population and 180 subjects were in the bmITT population at posttherapy (Days 13 to 17).

Efficacy results:
The primary efficacy assessment of clinical outcome at posttherapy for the PPb population showed that the clinical cure rate for telithromycin was 93.0% (66 of 71) and for penicillin 83.3% (70 of 84).

Safety results:
No deaths were reported during the study.

Treatment emergent adverse events were reported by 41.1% of subjects in the telithromycin group and 31.7% in the penicillin group. The most frequently reported treatment emergent adverse events in ≥3.0% subjects were: diarrhea (telithromycin: 9.8%, penicillin: 1.7%), vomiting (telithromycin: 3.6%, penicillin: 1.7%), nausea (telithromycin: 4.5%, penicillin: 4.2%), and headache (telithromycin: 4.5%, penicillin V: 0.8%).

One adolescent subject (0.9%) in the telithromycin group reported serious treatment emergent adverse events of serum sickness and liver function abnormality but recovered without sequelae. One adult subject (0.8%) in the penicillin group also reported a serious treatment emergent adverse event of visual tracking test abnormality and acute sinusitis, but recovered without sequelae. Treatment emergent adverse events leading to discontinuation were reported by 6.3% of subjects in the telithromycin group and 5.0% in the penicillin group.

Five (5) subjects in the telithromycin group and 2 subjects in the penicillin group reported hepatic adverse events of special interest. The elevation of alanine aminotransferase in 1 subject in the telithromycin group was reported as a serious treatment emergent adverse event. In the telithromycin group, 4 subjects had elevated levels of alanine aminotransferase. In these 4 subjects, 2 subjects had alanine aminotransferase >5 upper limit of normal (ULN) and 2 subjects had alanine aminotransferase within >3 and ≤5 ULN. In the subjects with >5 ULN, 1 subject also had elevated level of aspartate aminotransferase within >3 and ≤5 ULN. One subject in the telithromycin group had elevated level of bilirubin (1.7 ULN at Visit 1 and 1.5 ULN at Visit 3). In the penicillin group, 1 subject had elevated level of alanine aminotransferase within >3 and ≤5 ULN and 1 subject had elevated levels of aspartate aminotransferase (4.1 ULN). All subjects recovered without sequelae.

Three (3) subjects in each treatment group reported visual adverse events of special interest. In all the cases the events resolved without sequelae except for 1 adult subject with a mild event of blurred vision in the telithromycin group who had blurred vision with small print and was reported as ongoing. The event was attributed to the aging process and reported as not related to the study medication.

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