### 2.0 Synopsis

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<th>Abbott Laboratories</th>
<th>Individual Study Table Referring to Part of Dossier:</th>
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<td>Clarithromycin</td>
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**Title of Study:** Efficacy and Safety of Clarithromycin Suspension in the Treatment of Pediatric Acute Otitis Media

**Investigator:** On file.

**Study Site:** Multicenter (8 sites in Germany).

**Studied Period (Years):** April 1994 to April 1995  
**Phase of Development:** 3

**Objective:** The objective was to evaluate the efficacy and safety of clarithromycin suspension as treatment in children with acute otitis media.

**Methodology:** This was an open-label, multicenter, single-arm study of clarithromycin (Klacid Syrup) in children with acute otitis media. The patients received clarithromycin suspension 7.5 mg/kg body weight twice daily for 7 days. On Days 5 and 8 after the start of treatment, the physician monitored the child's health and documented any changes in symptoms and signs of acute otitis media. A final assessment was performed 28 days after the last treatment. Drug-related adverse events were recorded.

**Number of Subjects (Planned and Analyzed):** 102 patients enrolled, 98 analyzed for efficacy

**Diagnosis and Main Criteria for Inclusion:** Children enrolled in the study had acute otitis media. Children had to have at least 2 of the following symptoms required for a diagnosis of acute otitis media: otalgia, pulling or rubbing the ear, vomiting or diarrhea, fever, acute hearing impairment because of the otitis, or an upper respiratory tract infection, in each case in conjunction with the following signs: hyperemia of the eardrum, mobility-reduced or bulging eardrum, tympanic membrane with landmarks obscured, effusion or acute otorrhea for less than 24 hours. Typanometry could be used to confirm the diagnosis.

**Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number:** Clarithromycin (Klacid Syrup), 7.5 mg/kg body weight two times daily

**Duration of Treatment:** 7 days

**Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number:** None
Criteria for Evaluation:

**Efficacy:** For all patients, relief of symptoms of acute otitis media and the physician's evaluation of efficacy were used to evaluate clinical response to clarithromycin treatment. Otalgia was assessed on a 4-item pain scale with the following severities: none, mild, moderate, and severe.

**Safety:** Safety was assessed with drug-related adverse event reports.

Statistical Methods:
The percentage of patients with each of the following was calculated: reduction in ear pain, reduction in symptoms and signs observed, and clinical response, defined as cure and/or improvement.

Summary/Conclusions:
Of the 102 patients with acute otitis media enrolled in the study, 48 were male and 54 were female. Ages ranged from 2 months to 8 years. Thirty-three patients had a history of 1 or more otitis media infections over the past 12 months; 68 patients had no history of otitis media (for 1 patient, data was unavailable). In the majority of patients (73%), the otitis media was moderate; in 17%, severe, and in 10%, mild. At Baseline, 87 patients (85.3%) had 7 or more different symptoms and signs of acute otitis media, and 86 patients (84.3%) had moderate to severe ear pain. Four subjects were excluded from the efficacy analysis (2 for poor compliance and 2 for inclusion criteria violations).

**Efficacy Results:** The 98 patients analyzed displayed rapid improvement in ear pain. After 1 day of treatment, 71.5% of the patients experienced reduction in ear pain. After 2 days of treatment, 97% of patients experienced reduction in ear pain. There was also a significant reduction in the number of symptoms and signs observed.

Clinical response, defined as cure and/or improvement, was documented by the physicians for 97 patients (99%) on Day 5 of treatment. Treatment was discontinued in 1 patient.

**Safety Results:** Adverse events considered by the physicians to be directly related to treatment occurred in 3% of the patients (1 case of vomiting and 2 cases of allergic exanthema); 1 patient with allergic exanthema withdrew from the study. Four patients developed another respiratory tract infection within the 28-day follow-up period (3 had rhinitis, 1 had red eardrum).

Conclusions:
Clarithromycin suspension used for treatment of acute otitis media in children produced a clinical response in almost all of the children within 5 days of treatment, with a rapid resolution of ear pain and other symptoms. Clarithromycin suspension was considered to be an effective, rapidly acting, and well-tolerated antibiotic for the treatment of acute otitis media in children.

**Date of Synopsis:** Prepared on 22 Oct 2011 for submission to EMA in accordance with Article 45 of Regulation (EC) No 1901/2006. Date of original study report: Not available.