4 Program Overview

This section of the briefing document describes the clinical trials program for OTC Ome-Mg. Six adequate and well-controlled trials were conducted to evaluate the safety and effectiveness of Ome-Mg in both preventing and relieving heartburn (four trials evaluated Ome-Mg in preventing the occurrence of heartburn, and the remaining two trials evaluated the product's ability to relieve heartburn symptoms). Five consumer research trials were also conducted: one was a label comprehension trial and four evaluated consumer usage patterns among adults and adolescents in at-home OTC settings. The adequate and well-controlled clinical trials were conducted in volunteers 18 years of age and older, and the consumer research trials included volunteers 12 years of age and older.

Table 4.1 provides a summary of patient enrollment by treatment group and trial. A total of 11,644 patients participated across all trials; 8,563 subjects received either Omeprazole Magnesium 20.6 mg (Ome-Mg 20) or Omeprazole Magnesium 10.3 mg (Ome-Mg 10).

TABLE 4.1
SUMMARY OF SUBJECT EXPERIENCE ON OME-MG IN OTC CLINICAL TRIALS
INTENT-TO-TREAT SUBJECTS

Indication/Study Type	Single Dose			Multiple-Dose (Short-Term, ≤ 4 weeks)			Total
	10 mg	20 mg	Placebo	10 mg	20 mg	Placebo	
Prevention	815	826	813	1038	1047	1039	5578
Treatment	—	—	—	1244	1248	1229	3721
Consumer Usage							
Actual Use	—	—	—	489	825	—	1314
Adolescent Actual Use	—	—	—	—	92	—	92
Marketing	—	—	—	—	939	—	939
Total on Active Drug	815	826	—	2771	4151	—	8563
Total in Program	815	826	813	2771	4151	2268	11,644

4.1 Adequate and Well-Controlled Clinical Trials

Table 4.2 provides a summary of the six adequate and well-controlled trials that support safety and effectiveness in both heartburn prevention and relief.

Four studies investigated Ome-Mg's effectiveness in preventing heartburn. Two identical trials (Studies 171 and 183) evaluated the safety and effectiveness of Ome-Mg in preventing heartburn, regardless of the cause of heartburn, when administered daily during the morning over a 14-day period. The design of these two studies took into consideration (1) the pharmacokinetic (PK) and pharmacodynamic properties of PPIs (e.g., absorption); and (2) the mechanism of

action (PPIs reduce gastric acid secretion regardless of the stimulus). In addition, since prevention of meal-induced heartburn was the standard for evaluating the effectiveness of H_2RA medications, two identical trials (Studies 005 and 006) evaluated the ability of a single dose of Ome-Mg to prevent heartburn when administered 1 hour preceding a provocative meal. These four trials are discussed in Section 5.1 of this briefing document.

Identical Studies 092 and 095 evaluated the ability of Ome-Mg to relieve episodes of heartburn following the onset of symptoms. Since relief trials are generally considered to be the most difficult setting in which to prove efficacy of systemically-absorbed anti-secretory compounds (e.g., H_2-antagonists and PPIs), Trials 092 and 095 evaluated the ability of Ome-Mg to relieve heartburn symptoms after a single (first-treated) episode and across all treated episodes over a 14-day period.

Three additional single-dose trials (Studies 017, 018, and 019) were completed subsequent to filing the NDA. These trials are summarized in Appendix 2.

TABLE 4.2
LISTING OF ADEQUATE AND WELL-CONTROLLED CLINICAL TRIALS

Protocol Number	Type of Study	Study Design	Treatment	Duration of Treatment	Efficacy Measures	Total Number of Subjects Evaluated for Efficacy (ITT)
171	24-hr prevention of heartburn	Multi-center, double-blind, randomized, double-dummy, parallel, placebo-controlled	Ome-Mg 10, Ome-Mg 20, Placebo	1 week placebo run-in, 2 week treatment, 2 week placebo follow-up	Primary: • Heartburn-Free for 24 hours Secondary: • Nocturnal Heartburn • No More than Mild Heartburn • Heartburn occurrence (follow-up)	518 (Ome-Mg 10) 523 (Ome-Mg 20) 519 (Placebo)
183						520 (Ome-Mg 10) 524 (Ome-Mg 20) 520 (Placebo)
005	pre-prandial prevention of heartburn	Multi-center, double-blind, randomized, double-dummy, parallel, placebo-controlled	Ome-Mg 10, Ome-Mg 20, Placebo	1 week run-in, baseline meal, single dose, treatment meal	Primary: • Heartburn-Free for 4 hours Secondary: • Overall Assessment • Avg. Heartburn Severity over 4-Hour Post-Prandial Period • Maximum Severity Score • Reduction in Max. Severity Score from Baseline Meal • Backup Medication Use • Time to Taking Backup Med.	428 (Ome-Mg 10) 433 (Ome-Mg 20) 423 (Placebo)
006						387 (Ome-Mg 10) 393 (Ome-Mg 20) 390 (Placebo)
092	treatment of heartburn	Multi-center, double-blind, randomized, double-dummy, parallel, placebo-controlled	Ome-Mg 10, Ome-Mg 20, Placebo	1 week placebo run-in, 2 week treatment	Primary: • Sustained Complete Relief Secondary: • Overall Assessment • Sustained Adequate Relief • Complete Relief • Adequate Relief • Backup Medication Use • Time to Sustained Comp. Relief • Time to Complete Relief • Time to Taking Backup Med.	621 (Ome-Mg 10) 621 Ome-Mg 20) 627 (Placebo)
095						623 (Ome-Mg 10) 627 (Ome-Mg 20) 602 (Placebo)

4.2 Consumer Research Trials

Table 4.3 presents a summary of the consumer research trials. To aid in creating a label that promotes consumer understanding, one label comprehension study (Study 3358, no medication dispensed) and four trials that investigated consumer usage patterns in at-home settings were conducted among adults and adolescents. Three consumer usage studies were Actual Use trials (Studies 003, 022, and 067) investigating usage patterns based solely on reading the carton and package unit, while the remaining study also involved potential advertising (Study 014). Food and Drug Administration (FDA) input was incorporated into the Actual Use trial protocols. The label comprehension and consumer use trials are described in detail in Section 6 of this briefing document.

4.3 Heartburn Prediction Research

To complement the clinical efficacy program, additional research was conducted to determine the consumer's ability to predict heartburn occurrence in advance of the development of symptoms. The results are summarized in Appendix 1 of this document. This research verifies that heartburn sufferers who predict occurrence of heartburn on a given day, can do so with great accuracy. This accuracy supports that consumers who might take a preventive medicine in the morning on days they think heartburn will occur, would not be dosing needlessly.

TABLE 4.3
LISTING OF CONSUMER RESEARCH TRIALS

					Subjects		
Study ID	**Design**	**Dosing Duration**	**Study Endpoints**	**Treatment**	**Regimen**	**Received Medication**	**Safety**	**Usage Pattern**
003	SP, OL MD, MC	4 Weeks	Primary: Usage Patterns Secondary: EFF, OA	Ome-Mg 20	OD, prn	1,093	833	815
014	SP, OL MD, MC	4 Weeks	Primary: Usage Patterns Secondary: MV	Ome-Mg 20	OD, prn	1,440	939	896
022	SP, OL MD, MC	4 Weeks	Primary: Usage Patterns Secondary: EFF, OA	Ome-Mg 10	OD, prn	596	491	488
067	SP, OL MD, MC	4 Weeks	Primary: Usage Patterns Secondary: EFF, OA	Ome-Mg 20	OD, prn	100	92	92

DESIGN: SP = Single Product; OL = Open Label; MD = Multiple-Dose; MC = Multi-Center; OD = Once Daily; prn = As Necessary;
STUDY ENDPOINTS: EFF = Effectiveness Assessment = "Did the medication work for your heartburn?"; OA = Overall Assessment;
MV = Market Volume (Proprietary Information not Contained in NDA).