Effect of DocuSol® mini-enemas in the Treatment of Patients with Constipation

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Ethics and Regulatory Approval

Sponsor: Alliance Labs LLC. Date of Approval of the Final Protocol: 13 April 2015, Final date of Study: April 3, 2016. The study protocol and all its amendments, and the patient information sheet(s) were reviewed and approved by the appropriate independent ethics committees as detailed, Investigator: Mirela E. Ponduchi, MD, Ethics Committee: Compass IRB and/or Chesapeake IRB, Chairman(s): Chesapeake IRB Mitchell Reddish, PhD, Troy Priest, BA, JD Joy, Cavagnaro, PhD, DABT, RAC, Anita Tarzian, PhD, RN,

Additional international approvals; Compliance Statement/Attestation IRB Services attests that the above document(s) have been approved, as described above, and the membership of the IRB complies with the requirements defined in Health Canada regulations, 21 CFR parts 56 and 312.3 and 45 CFR 46. The IRB carries out its functions in accordance with good clinical practices (e.g., ICH GCP Guidelines) and Health Canada regulations and in compliance with FDA 21 CFR parts 50 and 56, DHHS 45 CFR part 46, and the Tri-Council Policy Statement for Ethical Conduct of Research Involving Humans, as appropriate to the research.

Summary:

Constipation is one of the most common functional bowel disorders encountered by health care providers. Disorders of constipation are associated with significant medical costs and a negative impact on quality of life. Although there is evidence supporting the effectiveness of some over-the-counter laxatives in constipation, currently there is no evidence supporting lifestyle modification or dietary change as effective long-term therapy for patients with constipation.

This single center, open-label study was conducted to determine the safety and efficacy of DocuSol® in patients with constipation. DocuSol® was shown to be highly effective in helping patients achieve bowel movements every other day, and free of any serious adverse effects. Currently DocuSol® is approved for treatment of general/occasional constipation for men and women over the age of 12 and is administered as a mini enema one to three times daily.

Additionally, this study highlights that the DocuSol® mini enema when used on an every other day basis, showed an improvement for managing constipation in all age groups, (25 to 65+ years) vs existing standard of care using other OTC or prescription laxatives. The data collected on patient satisfaction was found to be equal to five (of five) in all cases with the exception of one, in which a mean of 4.93 was indicated. These results indicate extremely high patient satisfaction associated with this product.

DocuSol® mini enema was shown to produce a bowel movement in an average of 10 minutes from application (see fig 1) and none of the patients included in the study were found to have experienced incontinent events. Not only was DocuSol® shown to reduce the occurrence of bowel incontinence, it did not cause inflammation or seepage of the mucosal lining of the lower bowel.

Category	N	Mean Evacuation Time (minutes)	SD
Age Group 25-54	3	9.82	8.37
Age Group 65+	31	9.97	7.18

Figure 1

Objective of the Study:

Length of time from the insertion of product to partial or complete evacuation. Number of episodes of incontinence per seven days, Ease of use, Patient Satisfaction, Length of time spent with patient by nurse for bowel care, number of dosing units required to gain an evacuation, reported adverse events: At time of dosing administration: cramping, abdominal pain, bleeding, rectal tear, discomfort, nausea, vomiting, rectal itching or burning of product. (these should not occur).

Clinical Overview:

DocuSol® (docusate sodium, 283mg) is a mini enema (5mL) intended for rectal administration. Docusate Sodium is an anionic surfactant with emulsifying, wetting and dispersing properties. It is classified pharmacologically as a stool softener laxative. Docusate has long been used to relieve constipation. A rectal enema dosage form offers a faster relief of constipation as well as an option for patients who experience issues with taking oral capsules, tablets, or syrup.

DocuSol® is comprised of one active and two inactive ingredients that are delivered directly to the receptor sites that typically promotes bowel movements within 2 - 15 minutes of administration. The active ingredient is docusate sodium and the inactive ingredients are polyethylene glycol and glycerin.

DocuSol® acts locally within the lower rectum to soften stools. The DocuSol® mini-enema lowers surface tension in the gastrointestinal tract, permitting water and fats to penetrate and soften fecal matter.

Patients:

This was a 30-day study with a minimum of 15 doses per patient. All patients had chronic constipation, defined as less than three bowel movements per week. Ninety percent (90%) of study population (27 patients) consisted of subjects 65-74 years of age and 10% (3 patients) were 75 years and older. A secondary control group of subjects 25-54 (3 patients) represented 10% of total study population.

Information on bowel movement frequency as well as chronic constipation history and treatments previously used were ascertained by interviewing the patients by a licensed physician or nurse practitioner. Patients were followed from the time of screening (initial dose) until 15 daily doses of study product had been self-administered (30 days from screening). Overall, 511 doses of DocuSol® mini-enema were recorded and evaluated.

In total, 45 treatments were in the 25-54 age group, with 466 in the 65+ age group. No significant mean differences were indicated between groups with respect to time or dosing units, while significant differences in these measures were not found on the basis of ethnicity or race. Common concurrent medical conditions consisted of diabetes, hyperlipidemia, hyperthyroidism, and hypertension, while concurrent medications were found to vary widely, with little oxycodone/narcotics use indicated.

Statistical Methodology:

The analyses conducted for this study consisted of descriptive statistics along with independent-samples t-tests and one-way ANOVAs. The descriptive statistics conducted consisted of frequency tables, reporting the sample sizes and percentages of response associated with each response category for the categorical measures of interest included within this study, along with measures of central tendency and variability calculated for the continuous items of interest included within this study. The mean was used as the measure of central tendency, with the standard deviation being calculated as the measure of variability. The independent-samples t-tests conducted focused upon mean differences in continuous outcomes comparing two groups of respondents, either the two groups of respondents formed based upon age category or ethnicity, with the one-way ANOVAs conducted focusing upon mean differences on the basis of respondent race.

Findings:

EFFICACY RESULTS:

With the use of bowel management protocols, the DocuSol® mini-enema showed an improvement for managing chronic constipation in the geriatric population in comparison to average age adults.

SAFETY RESULTS:

DocuSol® mini-enema has been shown to reduce the occurrence of bowel incontinence, and does not cause inflammation or seepage of the mucosal lining of the lower bowel.

Conclusions:

During this 'real world' study, the DocuSol® mini-enema provided consistent results within minutes of use. There were no conflicts based on a wide range of concurrent medication use, nor were any incontinent events reported.

The data collected on patient satisfaction was found to be equal to five (of five) in all cases with the exception of one, in which a mean of 4.93 was reported. These results indicate extremely high patient satisfaction associated with this product.

The full trial report may be obtained by contacting Alliance Labs at customerservice@alazinc.com

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