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COLLEGE OF MEDICINE
DEPARTMENT OF INTERNAL MEDICINE
DIVISION OF GASTROENTEROLOGY



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December 10, 1999

Lilia Talarico, M.D.
Food and Drug Administration
Division of Gastrointestinal Drug Products (HFD-180)
Document Control Room 6B-24
5600 Fishers Lane
Rockville, MD 20857

RE: Sodium Phosphate Based Bowel Preparations
Fleet Phospho-Soda
Inkine Diacol

Dear Dr. Talarico:

I have had a research interest in the sodium phosphate based bowel preparations for some years (Fleet Phospho-Soda and Inkine Diacol). In 1995 I published a study of biochemical changes in normal study subjects associated with a Phospho-Soda bowel preparation regimen as recommended by the manufacturer (copy enclosed). As expected, the study showed significant changes in serum electrolytes most notably in calcium and phosphorus. Unexpectedly, large increases in serum PTH and urine cAMP were observed that persisted even 24 hours after preparation. Obviously, the increases in PTH and cAMP occurred in response to the transient hyperphosphatemia and hypocalcemia induced by the ingested phosphate (it is well known that hyperphosphatemia and hypocalcemia are potent stimulants for PTH secretion).

Following completion of this study I wrote to Cheryl Turner in the Office of OTC drugs (copy enclosed) and stated that oral sodium phosphate is not safe for routine clinical use due to these significant biochemical effects. The most clinically significant of which is hypocalcemia (resulting from the hyperphosphatemia and subsequent soft tissue deposition of calcium phosphate). Indeed, there are numerous published reports of hypocalcemia resulting from oral Phospho-Soda bowel preparation (some of which resulted in death). A recent case report published in Diseases of the Colon and Rectum (copy enclosed) by Campisi et al now suggests that patients using bone metabolism regulators are particularly at risk. The report details a 24 year old Crohn's disease patient who developed severe hypophosphatemia and hypocalcemia resulting in tetany after bowel preparation with Phospho-Soda. This patient had been taking alendronate (known to induce mild decreases in serum calcium and phosphate levels)

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and as a result this patient had elevated PTH levels. The authors concluded that alendronate exacerbated the hypocalcemia induced by the Phospho-Soda preparation by inhibiting normal calcium mobilization from bone and they attribute the observed hypophosphatemia to the elevated PTH levels. As my research indicates, PTH levels will be further increased by the transient electrolyte changes induced by oral phosphate ingestion.

I remain convinced that the oral sodium phosphate bowel preparations are not safe for routine clinical use because they induce many biochemical changes. As the Campisi report indicates, these changes can have unexpected and sometimes disastrous effects. Many (if not most) patients requiring bowel preparation for diagnostic examination are elderly with reduced bone metabolic capacity. Such patients are ill equipped to withstand the biochemical effects of oral sodium phosphate ingestion. The addition of drugs like alendronate further reduces their capacity to respond to these changes. Therefore, I urge you to restrict these products from routine clinical use.

Sincerely,



Jack A. DiPalma, M.D.
Director, Division of Gastroenterology
Professor of Medicine

JAD/tb

CC: Cheryl Turner

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 1-5-2000

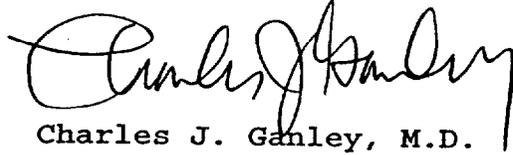
FROM: Director
Division of OTC Drug Products, HFD-560

SUBJECT: Material for Docket No. 78N-0364

TO: Dockets Management Branch, HFA-305

The attached material should be placed on public display under the above referenced Docket No.

This material should be cross-referenced to Comment No. _____


Charles J. Ganley, M.D.

Attachment

*please display attached as a
Comment.*

Sally Prescott (HFD-560)