DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINSTRATION	OPDRA POSTMARKETING SAFETY REVIEW	
TO: Charles Ganley, M.D., Division Director Division of Over-the-Counter Drug Products, HFD 560	**FROM: DDRE (HFD-4 30)** Claudia B. Karwoski, PharmD Safety Evaluator Team Leader	**OPDRA PID #** D020201

DATE REQUESTED: 5/15/02	**REQUESTOR/Phone #:** Linda Katz, M.D., Deputy Division Director Division of Over-the-Counter Drug Products, HFD 560	
DATE RECEIVED from DDRE PM: 4/27/02		
DRUG (Est):	**NDA/IND #** 009939	**SPONSOR**: Purdue Frederick
DRUG NAME (Trade): Senokot Granules	**THERAPEUTIC CLASSIFICATION:** Bulk laxatives	
EVENT: Esophageal obstruction and choking		

Executive Summary:

This document provides an update of our 2000 review of esophageal obstruction and related events associated with the use of psyllium products as well as providing information regarding these events with Senokot Granules. In our previous review, we found 98 cases of esophageal obstruction or choking associated with three different psyllium products (Perdiem-78, Metamucil-13, and Serutan-7). Since that time, we have received a follow-up to one report as well as a new report of esophageal obstruction with Perdiem.

Our search for all senna products including Senokot Granules, yielded two reports. One was a duplicate of a report previously evaluated. It was a literature report submitted by Purdue-Frederick but involved esophageal obstruction in a Parkinson's patient following the use of Perdiem (psyllium/senna).[1] The other was a report of a female who experienced "sustained choking episodes with after effects including vomiting and illnesses" following the use of Senokot Granules. This was a poorly documented report by the consumer's husband who was also an attorney. There was no mention of the woman requiring medical treatment.

The one report of possible choking with the use of Senokot Granules was not medically substantiated and did not provide sufficient information to determine the severity of the reaction and therefore does not provide evidence of esophageal obstruction or choking related problems with this product.

Reason for Request/Review: To support a proposal to reclassify the bulk-forming laxative psyllium ingredients in granular dosage form from Category I (safe and effective) to Category II (not safe and effective).

Relevant Product Labeling: See attachments 1 and 2

Usage Information: NA

Search Date: 5/9/02	**Search Type(s):** X AERS X Literature

AERS Search Criteria:

Senna or Sennoside Searches: We searched all years using the following terms: the higher level term (HLT) *esophageal stenosis and obstruction* and the preferred terms (PT) *choking sensation, dysphagia, dysphagia aggravated,* and *sensation of foreign body* linked to all senna or sennosides active ingredients. We also searched under the trade name Senokot, under the Senokot verbatim substances names, and by NDA numbers 009930 and 009939.

Psyllium Searches: The same search terms were used as above. We searched for those reports received after October 1, 2000 (time since last review) linked to all psyllium active ingredients. We also searched under the trade name Perdiem, Metamucil, and Serutan.

Search Results:

Senna or Sennoside Results: The above searches resulted in the 2 reports. One was a duplicate of a report included in the last document. It was a literature report submitted by Purdue-Frederick but involved esophageal obstruction in a Parkinson's patient following the use of Perdiem (psyllium/senna).

There was one report of a female (age unknown) who experienced "sustained choking episodes with after effects including vomiting and illnesses" following the use of Senokot Granules. This was a poorly documented report by the consumer's husband who was also an attorney. There was no mention of the woman requiring medical treatment.

Psyllium Results: We have received two reports since our first review. One report was a follow-up of a report of an 83-year-old female who experienced an esophageal obstruction after taking Perdiem. The follow-up was information received from the physician indicating that an esophagogastroduodenoscopy (EGD) was performed to remove the mass.

We received one new case (event year is 2001) of esophageal obstruction involving an 81-year-old male. He took one teaspoon with 8 ounces of water. He was unable to finish the water because he began to experience difficulty swallowing and began vomiting. He had difficulty sleeping that night and experienced the same symptoms the following day. He was taken to the emergency department and was subsequently hospitalized for two days.

Conclusion:

AERS contained one report of possible choking with the use of Senokot Granules and one additional report of esophageal obstruction with Perdiem since our previous review. The one report of possible choking with the use of Senokot Granules was not medically substantiated and did not provide sufficient information to determine the severity of the reaction and therefore does not provide evidence of esophageal obstruction or choking related problems with this product.

Reviewer's Signature / Date:

Division Director Signature / Date:

Reference:

1. Schulman LM, Minagar A, Weiner WJ. Perdiem causing esophageal obstruction in Parkinson's disease. Neurology 1999; 52: 670-1.

tachment 1-General Information regarding Senokot Granules

Use: Senokot Laxatives provide a virtually colon-specific action which is gentle, effective and predictable, generally producing bowel movement in 6 to 12 hours. SENOKOT has been found to be effective even in many previously intractable cases of functional constipation. SENOKOT preparations may aid in rehabilitation of the constipated patient by facilitating regular elimination. SENOKOT preparations enjoy high patient acceptance. Numerous and extensive clinical studies show their high degree of effectiveness in several types of functional constipation: geriatric and postpartum, drug-induced, pediatric, as well as in functional constipation concurrent with heart disease or anorectal surgery.

SENOKOT Granules: (cocoa-flavored): Each teaspoonful contains 15 mg sennosides. Active Ingredient: Standardized Senna Concentrate. Inactive Ingredients: Cocoa, Malt extract, Sodium lauryl sulfate, Sucrose, Vanillin and other ingredients.

There are no specific WARNINGS regarding the potential for Senokot granules to cause esophageal obstruction.

Senokot is also available in the following formulations:

SENOKOT Tablets: Each tablet contains 8.6 mg sennosides. Active Ingredient: Standardized Senna Concentrate. Inactive Ingredients: Cellulosic polymers, Corn starch, Glycerin, Lactose, Magnesium Stearate, Talc.
SenokotXTRA Tablets: Each tablet contains 17 mg sennosides. Active Ingredient: Standardized Senna Concentrate. Inactive Ingredients: Corn starch, Glycerin, Lactose, Magnesium stearate, Talc.
NOKOT-S Tablets: Each tablet contains 8.6 mg sennosides and 50 mg of docusate sodium. Active Ingredients: Docusate Sodium and Standardized Senna Concentrate. Inactive Ingredients: Cellulosic polymers, Corn starch, FD&C Yellow No. 10, FD&C Yellow No. 6 (Sunset Yellow), Guar Gum, Lactose, Magnesium stearate, Polyethylene glycol, Purified water, Talc, Titanium dioxide, and other ingredients.
SENOKOT Syrup (extract of senna concentrate) in bottles of 2 and 8 fl. oz. Each teaspoon of SENOKOT Syrup contains 8.8 mg sennosides. Active Ingredient: Extract of Senna Concentrate. Inactive Ingredients: Methylparaben, Natural and artificial flavors, Potassium sorbate, Propylene glycol, Propylparaben, Purified water, Sucrose.

Directions and Recommended Dose:

The recommended dose for Senokot Granules is provided in the table below. (May be eaten plain, mixed with liquids such as milk to make a delicious drink, or sprinkled on foods.):

AGE	STARTING	MAXIMUM
Adults and children 12 years of age and over	1 teaspoon once a day	2 teaspoons twice a day
6 to under 12 years of age	1/2 teaspoon once a day	1 teaspoon twice a day
2 to under 6 years of age	1/4 teaspoon once a day	1/2 teaspoon twice a day
Under 2 years	Consult a physician.	

Attachment 2-General Information regarding Perdiem Granules

Use: For relief of occasional constipation (irregularity)-generally in 12-72 hrs.

PERDIEM Granules: Active Ingredient: Each rounded (6 gram) teaspoonful contains psyllium 3.25g bulk fiber laxative Standardized Senna Concentrate. Inactive Ingredients: acacia, iron oxides, natural flavors, paraffin, sucrose, talc, titanium dioxide

CHOKING: TAKING THIS PRODUCT WITHOUT ADEQUATE FLUID MAY CAUSE IT TO SWELL AND BLOCK YOUR THROAT OR ESOPHAGUS AND MAY CAUSE CHOKING. DO NOT TAKE THIS PRODUCT IF YOU HAVE DIFFICULTY IN SWALLOWING. IF YOU EXPERIENCE CHEST PAIN, VOMITING, OR DIFFICULTY IN SWALLOWING OR BREATHING AFTER TAKING THIS PRODUCT, SEEK IMMEDIATE MEDICAL ATTENTION.

Do not use:

if you experience abdominal pain, nausea, or vomiting
if you have difficulty in swallowing
if you have esophageal narrowing

Directions:

Take this product (child or adult dose) with at least 8 ounces (a full glass) of cool water or other fluid. Taking this product without enough liquid may cause choking. See choking warning.

Perdiem should not be chewed.

1. Moisten your mouth with a drink of water or any cool beverage.
2. Place a teaspoonful of granules on your tongue. If you prefer, take only a partial teaspoonful at a time.
3. Without chewing, wash granules down with water or any cool beverage.
4. Repeat last three steps until the recommended dose has been swallowed. Be sure to drink at least 8 ounces of cool liquid.

Recommended Dose:

Adults and Children 12 years and older: In the evening and/or before breakfast, 1 to 2 rounded teaspoonfuls 1 to 2 times daily should be placed in the mouth and swallowed with at least 8 ounces of cool liquid.
Children 7 to 11 years: 1 rounded teaspoonful 1 to 2 times daily with at least 8 ounces of cool liquid

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: AUG - 4 2003

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

SUBJECT: Material for Docket No. 78N-036h

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