PRESCRIBING INFORMATION

LAX-A-DAY PHARMA™

Polyethylene Glycol 3350 Powder for Oral Solution

Laxative

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Polyethylene Glycol 3350 Powder for Oral Solution

THERAPEUTIC CLASSIFICATION

Laxative

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Oral	Powder for oral solution	None. *For a complete listing see Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

Adults

LAX-A-DAY PHARMA™ (Polyethylene Glycol 3350 Powder for Oral Solution) is indicated for:

- *Constipation*
  LAX-A-DAY PHARMA™ is indicated as a laxative for the treatment of occasional constipation. (See **DOSAGE AND ADMINISTRATION**).

CONTRAINDICATIONS

LAX-A-DAY PHARMA™ is contraindicated in patients with:

- known or suspected bowel obstruction, and
- known allergies to polyethylene glycol.

WARNINGS AND PRECAUTIONS

General

Patients with symptoms suggestive of bowel obstruction, appendicitis or inflamed bowels (fever, nausea, vomiting, abdominal pain or distention) should consult a doctor to rule out these conditions before initiating **LAX-A-DAY PHARMA™** therapy.

Overuse or extended use of any laxative may cause dependence for bowel function.

Do not take any type of laxative for more than one (1) week, unless recommended by a physician.

A laxative should not be taken within two (2) hours of another medicine because the desired effect of the other medicine may be reduced.

Patients presenting with complaints of constipation should have a thorough medical history and physical examination to detect associated metabolic, endocrine and neurogenic conditions, and medications. A diagnostic evaluation should include a structural examination of the colon. Patients should be educated about good defecatory and eating habits (such as high fiber diets) and lifestyle changes (adequate dietary fiber and fluid intake, regular exercise) which may produce more regular bowel habits.

LAX-A-DAY PHARMA™ should be administered after being dissolved in approximately 250 ml of water, juice, soda, coffee, or tea.

LAX-A-DAY PHARMA™ may result in a potential interactive effect when used with starch-based food thickeners. The PEG ingredient counteracts the thickening effect of starch, effectively liquefying preparations that need to remain thick for people with swallowing problems. This warning applies to all polyethylene glycol (PEG) containing-products.

Special Populations

Pregnant Women: Animal reproductive studies have not been performed with Polyethylene Glycol 3350. It is also not known whether Polyethylene Glycol 3350 can cause fetal harm when administered to a pregnant woman, or can affect reproductive capacity. The use of **LAX-A-DAY PHARMA™** should be avoided in women who are pregnant unless clearly needed and directed by a physician.

Nursing Women: It is unknown if **LAX-A-DAY PHARMA™** is excreted in human milk. Because many drugs are excreted in human milk, precaution should be exercised. The use of **LAX-A-DAY PHARMA™** should be avoided in nursing women unless clearly needed and directed by a physician.

Pediatrics (<18 years of age): Safety and effectiveness of **LAX-A-DAY PHARMA™** in pediatric patients has not been established.

Geriatrics (> 65 years of age): There is no evidence for special considerations when **LAX-A-DAY PHARMA™** is administered to elderly patients. If diarrhea occurs, **LAX-A-DAY PHARMA™** should be discontinued.

Monitoring and Laboratory Tests

No clinically significant effects (1,2,3,5,6) on laboratory tests have been demonstrated.

In one study (1), CBC, blood chemistry, and urinalysis were performed after the 14-day treatment period. Laboratory data were compared by repeated measures of analysis of variance. A value $p < 0.05$ was considered statistically significant. No statistically or clinically significant differences between placebo and laxative groups were detected for laboratory measurements.

In another study (2), CBC, blood chemistry, and urinalysis were performed before and after each10-day treatment period. No clinically significant changes in laboratory measurements were seen.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Occasionally, **LAX-A-DAY PHARMA™** may cause nausea, abdominal bloating, cramping, diarrhea and/or gas. High doses may produce diarrhea and excessive stool frequency, particularly in elderly nursing home patients.

On rare occasions, hives and skin rashes have been reported which are suggestive of an allergic reaction. Patients taking other medications containing polyethylene glycol have occasionally developed urticaria suggestive of an allergic reaction.

DRUG INTERACTIONS

No specific drug interactions have been demonstrated.

A laxative should not be taken within two (2) hours of taking another medicine because the desired effect of the other medicine may be reduced.

DOSAGE AND ADMINISTRATION

Recommended Dose and Dosage Adjustment

ADULTS:

The usual dose is 17 grams (about 1 heaping tablespoon or one single-dose sachet) of **LAX-A-DAY PHARMA™** powder per day (or as directed by physician) to be stirred in a cup (250 ml) of water, juice, soda, coffee, or tea until completely dissolved.

This product should be used for one week or less or as directed by a physician. Treatment for two to four days (48 to 96 hours) may be required to produce a bowel movement.

Each bottle of **LAX-A-DAY PHARMA™** is supplied with a dosing cap marked to contain 17 grams of laxative powder when filled to the indicated line. LAX-A-DAY PHARMA™ is also available in single-dose sachets of 17 grams each. Two to 4 days (48 to 96 hours) may be required to produce a bowel movement.

Special Patient Populations:

Treatment of Pregnant or Nursing Women
LAX-A-DAY PHARMA™ should only be administered to a pregnant or nursing woman on the advice of a physician. (See **WARNINGS AND PRECAUTIONS**).

Elderly Patients
No dose adjustment is recommended for elderly patients solely on the basis of their age (see **WARNINGS AND PRECAUTIONS**).

Pediatrics
LAX-A-DAY PHARMA™ is not indicated for use in children under 18 years of age unless recommended by a physician (See **WARNINGS AND PRECAUTIONS**).

OVERDOSAGE

There have been no reports of accidental overdosage. In the event of overdosage, diarrhea would be the expected major event. If an overdose of drug occurred without concomitant ingestion of fluid, dehydration due to diarrhea may result. In the event of overdose, medication should be terminated and free water administered.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Pharmacology:

Polyethylene Glycol 3350 is an osmotic agent which causes water to be retained with the stool.

Essentially, complete recovery of Polyethylene Glycol 3350 was shown in normal subjects without constipation. Attempts at recovery of Polyethylene Glycol 3350 in constipated patients resulted in incomplete and highly variable recovery.

An *in vitro* study showed indirectly that Polyethylene Glycol 3350 was not fermented into hydrogen or methane by the colonic microflora in human feces Polyethylene Glycol 3350 appears to have no effect on the active absorption or secretion of glucose or electrolytes. There is no evidence of tachyphylaxis.

Special Populations and Conditions

Pediatrics: The safety and efficacy of **LAX-A-DAY PHARMA™** for use in children under 18 years of age have not been established. **LAX-A-DAY PHARMA™** is not indicated for use in children under 18 years of age.

Geriatrics: There is no evidence for special considerations when **LAX-A-DAY PHARMA™** is administered to elderly patients. In geriatric nursing home patients a higher incidence of diarrhea occurred at the recommended 17 gram dose.

STORAGE AND STABILITY
Store at room temperature (15°C to 30°C).

SPECIAL HANDLING INSTRUCTIONS
None.

DOSAGE FORMS, COMPOSITION AND PACKAGING

LAX-A-DAY PHARMA™ is available in powdered form, for oral administration after complete dissolution in water, juice, soda, coffee, or tea. **LAX-A-DAY PHARMA™** is available in the following formats: bottles (119 g – 7 doses, 238 g – 14 doses, 510 g – 30 doses and 1020 g – 60 doses) and single-dose sachets of 17 g (available in packs of 10 and 100 sachets).

The dosing cap provided with each bottle is marked with a measuring line and should be used to measure a single daily dose of **LAX-A-DAY PHARMA™** (17 grams, or about 1 heaping tablespoon).

Composition of Product

Polyethylene Glycol 3350

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

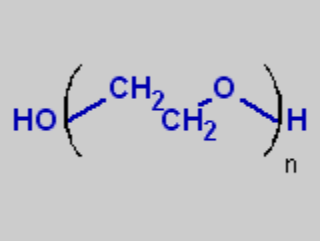
Proper name: Polyethylene Glycol 3350

Chemical name: Poly(oxy-1,2-ethanediyl), ∀-hydro-T-hydroxy-

Molecular formula: HO(C2H4O)nH
(n represents the average number of oxyethylene groups)

Molecular mass: average molecular weight of 3350 (The actual molecular weight is not less than 90.0 percent and not greater than 110.0 percent of the nominal value)

Structural formula:



Physical Form: A white powder for reconstitution

Solubility: Below 55°C it is a free flowing white powder freely soluble in water.

CLINICAL TRIALS

In two separate studies (1,3), 151 and 23 patients with less than 3 bowel movements per week were randomized to Polyethylene Glycol 3350, 17 grams, or placebo for 14 days. An increase in bowel movement frequency was observed for both treatment groups during the first week of treatment. Polyethylene Glycol 3350 was statistically superior to placebo during the first and second week of treatment. No clinically significant changes in blood chemistry, CBC, or urinalysis were observed. PEG laxative is safe and effective in the short term for the treatment of constipation.

In a second study (2), 50 patients with 3 bowel movements or less per week and/or less than 300 grams of stool per week were randomized to 2 dose levels of Polyethylene Glycol 3350 or placebo for 10 days each. Success was defined by an increase in both bowel movement frequency and daily stool weight. For both parameters, superiority of the 17gram dose of Polyethylene Glycol 3350 over placebo was demonstrated. There were no significant differences in laboratory changes or adverse experiences recorded between groups. PEG laxative is safe and effective in the short term treatment of constipation for ambulatory outpatients and is safe for long-term care patients.

In a fourth study (5), 304 patients with 3 bowel movements or less per week were randomized to 17 grams of Polyethylene Glycol 3350 or placebo for 6 months. Successful treatment according to the primary efficacy variable was seen in 52.0% of PEG and 11% of placebo subjects ($p < 0.001$). Similar efficacy was seen in a subgroup of 75 elderly subjects. According to the primary efficacy definition (based on individual treatment weeks), 61% of PEG treatment weeks versus 22% of the placebo weeks were successful ($p < 0.001$). There were no significant differences in laboratory findings of adverse events, except for the gastrointestinal category where diarrhea, flatulence, and nausea were the most frequent with PEG although they were not individually statistically significant compared to placebo. Similar results were observed when analyzed for differences due to gender, race or age. PEG laxative is safe and effective for use in patients with chronic constipation for 6 months.

In a fifth study (6), 24 adult patients aged > 19 years with a history of constipation were randomized to 3 dose levels of Polyethylene Glycol 3350 (51, 68 and 85 g) or placebo for a 24 hour period. Over a 72 hr period, subjects rated bowel movements, completeness of evacuation and satisfaction. There were no significant differences in laboratory changes or adverse experiences recorded between groups. A 68 g dose of PEG laxative seems to provide safe and effective relief in constipated adults within a 24 hour period.

TOXICOLOGY

Acute Toxicity:

The oral LD50 is >50 gm/Kg in mice, rats and rabbits.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Long term carcinogenicity studies, genetic toxicity studies and reproductive toxicity studies in animals have not been performed with Polyethylene Glycol 3350.

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