

PRESCRIBING INFORMATION

PegaLAX[®]

Polyethylene Glycol 3350
Powder for oral solution

100% w/w

Laxative

Aralez Pharmaceuticals Canada Inc.
7100 West Credit Avenue, Suite 101
Mississauga, ON
L5N 0E4

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PegaLAX®
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/100% w/w	None

INDICATIONS AND CLINICAL USE

Adults aged 18 years or older: PegaLAX, Polyethylene Glycol 3350 Powder for Oral Solution is indicated for the treatment of occasional constipation and irregularity. This product should be used for 7 days or less or as directed by a physician. PegaLAX reduces cramping and gas.

CONTRAINDICATIONS

PegaLAX is contraindicated in patients:

- with known or suspected bowel obstruction, and
- Known to be allergic to polyethylene glycol.

WARNINGS AND PRECAUTIONS

General

Patients with symptoms suggestive of bowel obstruction, appendicitis or inflamed bowel (fever, nausea, vomiting, abdominal pain or distension) should consult a doctor to rule out these conditions before initiating PegaLAX 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 should be instructed to consult their physician if unusual cramps, bloating or diarrhea occur.

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.

PegaLAX may result in a potential interactive effect when used with starch-based food thickeners. The polyethylene (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 PEG-containing products.

PegaLAX should be administered after being dissolved in approximately 250 ml of water, juice, soda, coffee or tea.

Special Populations

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

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

Pediatrics (<18 years of age): The safety and effectiveness **PegaLAX** in pediatric patients have not been established. **PegaLAX** should not be used in children under 18 years of age.

Geriatrics (>65 years of age): There is no evidence for special considerations when **PegaLAX** is administered to elderly patients. In geriatric nursing home patients, a higher incidence of diarrhea occurred at the recommended 17 g dose. If diarrhea occurs, **PegaLAX** should be discontinued.

Monitoring and Laboratory Tests

No clinically significant effects on laboratory tests have been demonstrated.

ADVERSE REACTIONS

PegaLAX 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 another medicine because the desired effect of the other medication may be reduced.

DOSAGE AND ADMINISTRATION

Recommended Dose and Dosage Adjustment

Adults aged 18 years or older: The usual dose is 17 grams (about 1 heaping tablespoon) of **PegaLAX** 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.

Do not take any type of laxative for more than one week, unless your physician has ordered a special schedule for you.

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.

PegaLAX should be used once a day only.

Administration

Oral

Reconstitution:

Oral Solutions:

- **PegaLAX** is packaged into sachets.
- Each sachet contains 17 grams of **PegaLAX** powder for oral solution.
- The usual daily dose of **PegaLAX** powder (17 grams) should be stirred in 250 ml or 8 ounces of water, juice, soda, coffee or tea until completely dissolved.
- Then solution should be drunk immediately;

Special Patient Populations:

Treatment of Pregnant or Nursing Women

PegaLAX 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

PegaLAX 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 over dosage. In the event of over dosage diarrhea would be the expected major event. If an overdose of drug occurred without concomitant ingestion of fluid, dehydration due to diarrhea may result. Medication should be terminated and plenty of water should be administered. For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

PegaLAX (polyethylene glycol 3350, powder for oral solution) is a synthetic polyglycol having an 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. The chemical formula is $\text{HO}(\text{C}_2\text{H}_4\text{O})_n\text{H}$ in which n represents the average number of oxyethylene groups. Below 55°C it is a free flowing white powder freely soluble in water. **PegaLAX** is an osmotic agent for the treatment of constipation. **PegaLAX** softens the stool and increases the frequency of bowel movements by retaining water in the stool.

Pharmacology:

PegaLAX is an osmotic agent which causes water to be retained with the stool. Essentially, complete recovery of **PegaLAX** was shown in normal subjects without constipation. Attempts at recovery of **PegaLAX** 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 micro flora in human feces. **PegaLAX** appears to have no effect on the active absorption or secretion of glucose or electrolytes. There is no evidence of tachyphylaxis.

Pharmacodynamics

Pharmacotherapeutic group: A06A D15

Polyethylene Glycol 3350 exerts an osmotic action in the gut, which induce a laxative effect. PEG 3350 increases the stool volume, which triggers colon motility via neuromuscular pathways. The physiological consequence is a propulsive colonic transportation of the softened stools.

Pharmacokinetics

Polyethylene glycol 3350 is unchanged along the gut. It is virtually unabsorbed from the gastrointestinal tract. Any PEG 3350 that is absorbed is excreted via the urine

Special Populations and Conditions

Pediatrics: The safety and efficacy of **PegaLAX** for use in children under 18 years of age have not been established. **PegaLAX** is not indicated for use in children under 18 years of age.

Geriatrics: There is no evidence for special considerations when **PegaLAX** is administrated to elderly patients. In geriatrics nursing home patients, a higher incident of diarrhea occurred at the recommended 17gram dose.

STORAGE AND STABILITY

Store at 15-30° C, in dry area. Keep out of reach of children.

Shelf life period: 2 years

DOSAGE FORMS, COMPOSITION AND PACKAGING

PegaLAX is a white powder of 100% of Polyethylene Glycol 3350.

PegaLAX powder for oral solution is supplied in:

A laminated low density polyethylene/aluminum/low density polyethylene/paper sachet containing 17 gram of white powder.

14 sachets are placed in a cardboard carton.

There are no non-medicinal ingredients.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

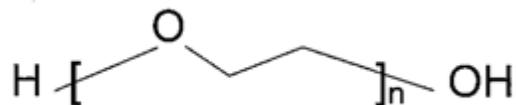
Drug Substance

Proper name: Polyethylene Glycol 3350

Chemical name: Polyethylene glycol 3350

Molecular formula and molecular mass: $\text{H}(\text{C}_2\text{H}_4\text{O})_n\text{OH}$,
3350 (n=76)

Structural formula:



Empirical Formula: $\text{HOCH}_2(\text{CH}_2\text{OCH}_2)_n\text{CH}_2\text{OH}$
Where 'n' represents the average number of oxyethylene groups.

Structural formula: $\text{HOCH}_2 - (\text{CH}_2 - \text{O} - \text{CH}_2)_n - \text{CH}_2\text{OH}$

Physicochemical properties: White or almost white solid with a waxy or paraffin-like appearance.
Solubility in water: Very soluble in water and in methylene chloride, very slightly soluble in alcohol, practically insoluble in fatty oils and in mineral oils.

CLINICAL TRIALS

Polyethylene glycol (PEG) is an osmotic laxative, relieving constipation by drawing water into the intestinal lumen. This results in softer stools and an increase in the frequency of bowel movements, thereby allowing bowel movements to occur more normally.

Compiling results from 37 clinical trials of the safety and efficacy of various treatments for constipation, a systematic review concluded that PEG had good evidence to support its use in patients with constipation, with consistent results from well-designed, well-conducted studies¹. In a 2-week, randomized, double-blind, placebo-controlled trial of 23 patients also found that PEG 3350 product significantly increased bowel movement frequency. Additionally, PEG 3350

product was associated with easier passage and softer stools as well as less cramping and less rectal irritation, compared with placebo².

In another 2-week, randomized, double-blind, placebo-controlled trial of 151 people with constipation, those taking a PEG 3350 product had significantly more bowel movements than did those taking placebo. Additionally, during the treatment period, significantly fewer people in the PEG3350 group reported hard stool consistency or difficult passage, severe cramping, or severe gas when compared with placebo³.

From another open-label, single-product, multicenter study, self-controlled studies where 74 patients with constipation used PEG 3350 product instead of their usual laxative for up to 2 weeks, it has been reported that there were no serious adverse events reported, events observed, such as loose stools, were mild and expected, bowel movement frequency was nearly doubled after PEG 3350 use⁴.

The safety and effectiveness of PEG 3350 product in 50 people with constipation who were either ambulatory outpatients or living in long-term care facilities were evaluated in two randomized cross-over clinical trials at different sites. Patients received placebo or a high (34 grams) or low (17 grams) dose of PEG 3350 product (later reduced to 12 and 6 grams, respectively, in long-term care patients). All patients given PEG 3350 product had increases in how often they had bowel movements and improvement in the quality of the bowel movement, with no severe side effects. The higher doses of PEG 3350 product yielded better bowel movements more often versus lower doses, and people given either dose of PEG 3350 product had better outcomes than those on placebo⁵.

PegaLAX is a safe and effective option for the treatment of constipation. Generally, it produces a bowel movement within 2-4 days (48 to 96 hours). It is available as a tasteless, grit-free powder that can be mixed with any beverage and taken once each day. Pharmacists should ensure that patients are using **PegaLAX** for the short-term treatment of constipation and should refer individuals to a primary care provider for further evaluation if symptoms persist beyond 1 week.

TOXICOLOGY

Acute Toxicity

PEGs themselves have been shown to have very low toxicity. The acute oral toxicity (LD₅₀) for Polyethylene Glycol 3350 is 4000mg/Kg in rats.

Carcinogenesis, Mutagenesis and Impairment of Fertility

Long term carcinogenicity studies, genetic toxicity studies and reproductive toxicity studies in animals have not been performed with **PegaLAX**.

REFERENCES

1. Ramkumar D, Rao SSC. Efficacy and safety of traditional medical therapies for chronic constipation: systematic review. *Am J Gastroenterol*. 2000; 95:446-50.
2. Cleveland MV, Flavin DP, Ruben RA, et al. New polyethylene glycol laxative for treatment of constipation in adults; a randomized, double-blind, placebo-controlled study. *South Med J*. 2001; 94: 478-81.
3. DiPalma JA, DeRidder PH, Orlando RC, et al. A randomized, placebo-controlled, multicenter study of the safety and efficacy of a new polyethylene glycol laxative. *Am J Gastroenterol*. 2000; 95: 446–50.
4. An Efficacy and Consumer Preference Study of Polyethylene Glycol 3350 for the Treatment of Constipation in Regular Laxative Users. *Home Health Care Consultant* 2001;8[2]:21-26.
5. Braintree Polyethylene Glycol (PEG) Laxative for Ambulatory and Long-Term Care Facility Constipation Patients. DiPalma JA et al. *Online Journal of Digestive Health*. 1999;1(2).

PART III: CONSUMER INFORMATION

PegaLAX[®]

Polyethylene Glycol 3350 powder for oral solution

This leaflet is part III of a three-part "Prescribing Information" published when PegaLAX was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about PegaLAX. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Adults aged 18 years or older: PegaLAX relieves occasional constipation and irregularities. It reduces cramping and gas.

What it does:

Polyethylene Glycol 3350 powder for oral solution softens the stool and increases the frequency of bowel movements by retaining water in the stool.

When it should not be used:

DO not take PegaLAX if you suspect or your doctor suspects:

- You have an obstruction in your intestine (gut).
- You are allergic (hypersensitive) to Polyethylene glycol 3350.

What the medicinal ingredient is:

100% Polyethylene Glycol 3350

What the important nonmedicinal ingredients are:

None

What dosage forms it comes in:

PegaLAX is available in powder form for oral administration after dissolution in water, juice, soda, coffee or tea.

PegaLAX is available in one package size:

17 g powder contained in sachet with 14 sachets packed in a carton.

WARNINGS AND PRECAUTIONS

Before you use PegaLAX, talk to your doctor or pharmacist if you:

- are allergic to polyethylene glycol or any other medication;
- are pregnant, plan to become pregnant, or are breastfeeding. If you become pregnant while taking polyethylene glycol 3350, call your doctor;
- have any kidney problems;

- have or have ever had a bowel obstruction (blockage in the intestine);
- have symptoms of bowel obstruction (fever, nausea, vomiting, stomach pain or bloating).
- have any tendency to regurgitate (bring up) food from the stomach into your esophagus or any tendency to accidentally inhale food or regurgitate food into the airways. PegaLAX contains polyethylene glycol (PEG), which may stop starch-based food thickeners from working. This may cause certain mixtures to be watery and difficult to swallow.

While taking PegaLAX:

- Take PegaLAX exactly as directed because overuse or extended use may cause dependence for bowel function;
- Do not use for more than 7 days;
- Stop use and contact a doctor immediately if:
 - Unusual cramps, bloating or diarrhea occur.
 - Your condition persists or worsens.
 - You do not have a bowel movement within two to four days of taking PegaLAX.

PegaLAX should not be used in children under 18 years of age.

INTERACTIONS WITH THIS MEDICATION

No specific drug interactions have been demonstrated.

Taking other medicines

Do not take PegaLAX within two (2) hours of taking another medicine because the desired effect of the other medicine may be reduced.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription, vitamins, nutritional supplements and herbal products.

PROPER USE OF THIS MEDICATION

Always take PegaLAX exactly as directed. Check with your doctor or pharmacist if you are not sure.

Usual dose (**Adults 18 years of age and older**): Use one dose (17g) once a day.

Children under 18 years: **Do Not use.**

Directions:

1. Stir the content of one sachet (17g) or 1 measuring scoop or dosing cup (filled up to the indicated line) in a cup (250 ml) of water, juice, soda, coffee or tea until completely dissolved,

2. Drink solution immediately.

Treatment for two to four days (48 to 96 hours) may be required to produce a bowel movement.

Do not take this product for more than one week, unless your physician has ordered a special schedule for you.

PegaLAX should be used once a day only. Taking more than the prescribed dose may cause loss of fluid due to severe diarrhea.

Overdose:

There have been no reports of accidental over dosage.

In case of overdose, stop taking PegaLAX, drink plenty of water and contact a physician or poison control centre immediately even if there are no symptoms.

Missed Dose:

If you forget to take PegaLAX, take the dose as soon as you realize you have not taken it.

If you have any further questions on the use of this product, ask your doctor or pharmacist

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptoms / Effects		Talk with your doctor or pharmacist right away		Seek urgent medical attention
		Only if severe	In all cases	
	itching, swelling of the lips, face, tongue, throat, trouble breathing, wheezing, shortness of breath, skin rashes, blisters of the skin, sore or pain in the mouth or eyes)			

This is not a complete list of side effects. For any unexpected effects while taking PegaLAX contact your doctor or pharmacist.

HOW TO STORE IT

Keep out of the reach of children.

Do not use PegaLAX after the expiry date which is stated on the carton and sachets.

The expiry date refers to the last day of the month.

Keep PegaLAX at temperature between 15°C -30°C in dry area.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, PegaLAX can have side effects although not everyone will get them.

Some side effects of PegaLAX are:

- Nausea, abdominal bloating, cramping and gas,
- Diarrhea especially if elderly.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptoms / Effects		Talk with your doctor or pharmacist right away		Seek urgent medical attention
		Only if severe	In all cases	
Common	Nausea, abdominal bloating, cramping and gas	✓		
Uncommon	Diarrhea	✓		
Rare	Allergic reactions (red skin, hives,			✓

Reporting Suspected Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<http://www.hc-sc.gc.ca/dhpm/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

Remember: Only a doctor can prescribe it for you. Never give it to someone else.

This leaflet does not contain the complete information about your medicine. If any questions remain unanswered or you are not sure about something, you should ask your doctor or pharmacist.

This document plus the full prescribing information, prepared for health professionals can be found at:

<http://www.aralez.com> or by contacting the sponsor,

Aralez Pharmaceuticals Canada Inc.
7100 West Credit Avenue, Suite 101
Mississauga, ON L5N 0E4, at:
1-866-391-4503.

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