normalax™
Polyethylene glycol 3350

Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT
Normalax

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
100% Polyethylene glycol 3350.

3. PHARMACEUTICAL FORM
Powder for oral solution.
White to creamy white powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
For the treatment of constipation.

4.2 Posology and method of administration

Oral use.

Adults and Children over 8 years:
17g dissolved in about 230ml (1 cup) of any chosen beverage, once daily, preferably taken as a single dose in the morning.
The effect of Normalax becomes apparent within 24-48 hours after its administration.

Pediatric population:

6 months to 1 year	4 grams per day
1 year to 4 years	4-8 grams per day
From 4 years to 8 years	8-16 grams per day

Each 4 gram dose should be dissolved in approximately 50 ml of any chosen beverage (including baby formula) just before use.

When more than 4 grams are required the dose can be divided and taken twice daily – morning and evening.

Treatment-induced restoration of bowel movements will be maintained by lifestyle and dietary measures.

The daily dose for children should be adapted according to the clinical response and may range from 4 grams to 16 grams a day.
The effect of Normalax becomes apparent within 24-48 hours after its administration.
In children, treatment should not exceed 3 months due to a lack of clinical data for treatment lasting longer than 3 months.

4.3 Contraindications

- Hypersensitivity to polyethylene glycol (macrogol).
- Severe inflammatory bowel disease (such as ulcerative colitis, Crohn's disease) or toxic megacolon, associated with symptomatic stenosis,
- Digestive perforation or risk of digestive perforation,
- Ileus or suspicion of intestinal obstruction,
- Painful abdominal syndromes of indeterminate cause.

4.4 Special warnings and precautions for use

The treatment of constipation with any medicinal product is only an adjuvant to a healthy lifestyle and diet, for example:

- Increased intake of liquids and dietary fiber,
- Appropriate physical activity and rehabilitation of the bowel reflex.

In case of diarrhea, caution should be exercised in patients who are prone to a disturbance of water electrolyte balance (e.g. the elderly, patients with impaired hepatic or renal function or patients taking diuretics) and electrolyte control should be considered.

Hypersensitivity reactions (rash, urticaria and oedema) have been reported with drugs containing polyethylene glycol (macrogol). Exceptional cases of anaphylactic shock have been reported.

Normalax contains a non-significant amount of sugar or polyol and thus may be prescribed to diabetic patients or patients on a galactose-free diet.

According to the way of action of polyethylene glycol, it is recommended to intake liquids during the treatment with this medicine (please see section 5.1).

The absorption of other medicinal products could transiently be reduced due to an increase in gastro-intestinal transit rate induced by polyethylene glycol (see section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

There is a possibility that the absorption of other medicinal products could be transiently reduced during use with Normalax. The therapeutic effect of medicinal products with a narrow therapeutic index may be particularly affected (e.g. antiepileptics, digoxin and immunosuppressive agents).

4.6 Fertility, pregnancy and lactation

<u>Pregnancy</u>

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

There are limited amount of data (less than 300 pregnancy outcomes) for the use of Normalax in pregnant women.

No effects during pregnancy are anticipated, since systemic exposure to Normalax is negligible. Normalax can be used during pregnancy.

<u>Lactation</u>

There are no data on the excretion of Normalax in breast milk. No effects on the breast fed newborn/infant are anticipated since the systemic exposure of the breast-

feeding woman to polyethylene glycol is negligible. Normalax can be used during breast feeding.

Fertility:

No fertility studies were conducted with Normalax however since polyethylene glycol is not significantly absorbed no effects are anticipated.

4.7 Effects on ability to drive and use machines

Normalax has no influence on ability to drive and use machines.

4.8 Undesirable effects

Undesirable effects are listed under headings of frequency using the following categories:
Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

Adult population:
The undesirable effects listed in the table below have been reported during clinical trials (including 600 adult patients) and post-marketing use. Generally, adverse reactions have been minor and transitory and have mainly concerned the gastrointestinal system:

System Organ Class	Adverse reactions
Immune system disorders	
Very rare	Hypersensitivity reactions (pruritus, rash, face oedema, Quincke oedema, urticaria, anaphylactic shock)
Not known	Erythema
Metabolism and Nutrition Disorders	
Not known	Electrolytes disorders (hyponatremia, hypokalaemia) and/or dehydration, especially in elderly patients
Gastrointestinal disorders	
Common	Abdominal pain and/ or distension Diarrhea Nausea
Uncommon	Vomiting Urgency to defecate Fecal incontinence

Paediatric population:
The undesirable effects listed in the table below have been reported during clinical trials including 147 children aged from 6 months to 15 years and post-marketing use.

As in adult population, adverse reactions have generally been minor and transitory and have mainly concerned the gastrointestinal system:

System Organ Class	Adverse reactions
Immune system disorders	
Not known	Hypersensitivity reactions (anaphylactic shock, angioedema, urticaria, rash, pruritus)
Gastrointestinal disorders	
Common	Abdominal pain Diarrhea*
Uncommon	Vomiting Bloating Nausea

* Diarrhea may cause perianal soreness

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions by using an online form
https://sideeffects.health.gov.il/

4.9 Overdose
Overdose could lead to diarrhea which disappears when treatment is temporarily interrupted or the dosage is reduced.
Excessive fluid loss by diarrhea or vomiting may require correction of electrolyte disturbances.
Cases of aspiration have been reported when extensive volumes of polyethylene glycol (macrogol) and electrolytes were administered with nasogastric tube. Neurologically impaired children who have oromotor dysfunction are particularly at risk of aspiration.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Osmotically acting laxatives

ATC code: A06AD15
High molecular weight (3350) polyethylene glycols are long linear polymers which retain water molecules by means of hydrogen bonds. When administered by the oral route, they lead to an increase in volume of intestinal fluids.
The volume of unabsorbed intestinal fluid accounts for the laxative properties of the solution.

5.2 Pharmacokinetic properties

The pharmacokinetic data confirm that polyethylene glycol undergoes neither gastrointestinal resorption nor biotransformation following oral ingestion.

5.3 Preclinical safety data
Toxicological studies in different animal species did not reveal any signs of systemic or local gastrointestinal toxicity. Polyethylene glycol had no teratogenic or mutagenic effect.
No carcinogenicity studies have been performed.
Polyethylene glycol was not teratogenic in rats or rabbits.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
No excipients

6.2 Incompatibilities
Not applicable

6.3 Shelf life
The expiry date of the product is indicated on the packaging materials. The bottle pack can be used within 12 months after opening.

6.4 Special precautions for storage
Store below 25°C

6.5 Nature and contents of container
Bottles containing 70g and 240g.
Sachets containing 17g.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
No special requirements

7. MARKETING AUTHORISATION HOLDER
Taro Pharmaceutical Industry Ltd.
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This leaflet was revised in January 2024 according to MOH guidelines