

Exhibit F

Approved (Translated) Labels in Portugal

(7.5 mg/ml drops; 2.5 mg capsules)

PACKAGE LEAFLET

02 June, 2000

GUTTALAX®

Sodium picosulphate

Contact laxative

Qualitative and quantitative composition

1 ml solution(= 15 drops) contains 7.5 mg
of 4,4'-(2-pyridyl-methylene)-diphenol-bis(hydrogen sulphate-ester)disodium salt
(sodium picosulphate)

Pharmaceutical form and contents

Oral solution
Drop-counter vial with 30 ml of solution

Pharmacotherapeutic group

VII – 5.b. Gastrointestinal track drugs. Laxatives. Contact laxatives

Properties

Sodium picosulphate, the active ingredient of **Guttalax®** is a locally acting laxative from the triarylmethane group. After bacterial cleavage in the colon stimulates the mucosa of the large intestine, causing colonic peristalsis.

Marketing authorization holder

Boehringer Ingelheim, Lda.
Av. António Augusto de Aguiar, 104-1º
1069-029-Lisboa
Representative of Boehringer Ingelheim International GmbH

Therapeutic indications

For use in cases of constipation and in conditions which require defecation to be facilitated.

Contraindications

Guttalax® is contraindicated in patients with ileus, intestinal obstruction, acute surgical abdominal conditions such as appendicitis, acute inflammatory bowel diseases, and in severe dehydration.

Guttalax® is also contraindicated in patients with known hypersensitivity to sodium picosulphate or any other component of the product.

Side effects

Abdominal discomfort and diarrhoea have been reported rarely.

Drug interactions and other forms of interaction

The concomitant use of diuretics or adreno-corticosteroids may increase the risk of electrolyte imbalance if excessive doses of **Guttalax®** are taken.

Electrolyte imbalance may lead to increased sensitivity to cardiac glycosides.

Special warnings and precautions

As with all laxatives, **Guttalax®** should not be taken on a continuous daily basis for long periods. If it is verified that laxatives are needed every day, the cause of constipation should be investigated.

Prolonged or excessive use may lead to fluid and electrolyte imbalance and hypokalaemia, and may precipitate onset of rebound constipation.

Children should not take **Guttalax®** without medical advice.

Pregnancy and lactation

Long experience has shown no evidence of undesirable or damaging effects during pregnancy. Nevertheless, as with all drugs, **Guttalax®** should only be taken during pregnancy on medical advice.

Even though there is no evidence that **Guttalax®** may enter breast milk, breast-feeding is not recommended.

Effects on ability to drive and use machines

No effects were observed on the ability to drive and use machines.

Warning: contains parabenes.

Posology and method of administration

Unless otherwise prescribed by the physician, the following dosages are recommended:

Adults and children over 10 years:	10 - 20 drops (5 - 10 mg)
Children 4 - 10 years:	5 - 10 drops (2.5 - 5 mg)

For children under 4 years of age, the recommended dosage is 0,250 mg per kilogram body weight.

Guttalax® should be taken at night to produce evacuation the following morning.

Overdose

Symptoms

If high doses are taken, **Guttalax®** can cause watery stools (diarrhoea), abdominal cramps and a clinically significant loss of potassium and other electrolytes.

Furthermore cases of colonic mucosal ischaemia have been reported in association with high doses of **Guttalax®** (considerably higher than those recommended constipation).

Laxatives in chronic overdose are known to cause chronic diarrhoea, abdominal pain, hypokalaemia, secondary hyperaldosteronism and renal calculi. Renal tubular damage, metabolic alkalosis and muscle weakness secondary to hypokalaemia have also been described in association with chronic laxative abuse.

Therapy

Drug absorption can be prevented or minimised if short after ingestion vomiting is induced or gastric lavage is made. Replacement of fluids and correction of electrolyte imbalance may be required. This is especially important in the elderly and the young.

Administration of antispasmodics may be of some value.

Recomendations

Inform your doctor or pharmacist of undesirable effects occurred with this drug and which are not described in this package leaflet.

Check the expiry date before using this drug.

Keep well corked and protected from light and heat.

Keep drugs out of the reach of children.

Last revision date of this package leaflet

February 2000

PACKAGE LEAFLET

26 April, 2003

GUTTALAX® CÁPSULAS

Contact laxative

Soft capsule

This package leaflet contains important informations for you. Read it carefully. This drug can be obtained without medical prescription and is intended to treat diseases which can be treated without doctor's assistance. Nevertheless, one should use **Guttalax® Capsulas** with precaution in order to obtain the proper results.

Keep this package leaflet. You may have the need to read it again.
In case further clarifications or advice are needed ask the pharmacist's assistance.
In case of health condition worsening or non recovery after 7 days consult your doctor.

Qualitative and quantitative composition

A capsule contains 2.5 mg
of 4,4'-(2-pyridyl-methylene)-diphenol-bis(hydrogen sulphate-ester)disodium salt
(sodium picosulphate)

Pharmacotherapeutic group

VII – 5.b. Gastrointestinal track drugs. Laxatives. Contact laxatives

Pharmaceutical form and contents

Capsules.
Package of 30 soft gelatin capsules.

Properties

Sodium picosulphate, the active ingredient of **Guttalax® Capsulas** is a locally acting laxative from the triarylmethane group. After bacterial cleavage in the colon stimulates the mucosa of the large intestine, causing colonic peristalsis.

Marketing authorization holder

Boehringer Ingelheim, Lda.
Av. António Augusto de Aguiar, 104-1º
1069-029-Lisboa

Therapeutic indications

For use in cases of constipation and in conditions which require defecation to be facilitated.

Contraindications

Guttalax® Capsulas is contraindicated in patients with ileus, intestinal obstruction, acute surgical abdominal conditions such as appendicitis, acute inflammatory bowel diseases, and in severe dehydration.

Guttalax® Capsulas is also contraindicated in patients with known hypersensitivity to sodium picosulphate or any other component of the product.

Side effects

Abdominal discomfort and diarrhoea have been reported rarely.

Drug interactions and other forms of interaction

The concomitant use of diuretics or adreno-corticosteroids may increase the risk of electrolyte imbalance if excessive doses of **Guttalax® Capsulas** are taken.

Electrolyte imbalance may lead to increased sensitivity to cardiac glycosides.

Special warnings and precautions

As with all laxatives, **Guttalax® Capsulas** should not be taken on a continuous daily basis for long periods. If it is verified that laxatives are needed every day, the cause of constipation should be investigated.

Prolonged or excessive use may lead to fluid and electrolyte imbalance and hypokalaemia, and may precipitate onset of rebound constipation.

Chronic use of this drug can bear health risks.

Children should not take **Guttalax® Capsulas** without medical advice.

Pregnancy and lactation

Long experience has shown no evidence of undesirable or damaging effects during pregnancy. Nevertheless, as with all drugs, **Guttalax® Capsulas** should only be taken during pregnancy on medical advice.

Even though there is no evidence that **Guttalax® Capsulas** may enter breast milk, breast-feeding is not recommended.

Effects on ability to drive and use machines

No effects were observed on the ability to drive and use machines.

Excipients list

Propylenoglycol and macrogol 400.

Posology and method of administration

Unless otherwise prescribed by the physician, the following dosages are recommended:

Adults and children over 10 years:	2 - 4 capsules (5 - 10 mg)
Children 4 - 10 years:	1 - 2 capsules (2.5 - 5 mg)

For children under 4 years of age, the recommended dosage is 0,250 mg per kilogram body weight.

Guttalax® Capsulas should be taken at night to produce evacuation the following morning.

Capsules should be swallowed with a bit of water.

Guttalax® Capsulas should not be used for a period of time superior to 7 days.

Overdose

Symptoms

If high doses are taken, **Guttalax® Capsulas** can cause watery stools (diarrhoea), abdominal cramps and a clinically significant loss of potassium and other electrolytes.

Furthermore cases of colonic mucosal ischaemia have been reported in association with high doses of **Guttalax® Capsulas** (considerably higher than those recommended constipation).

Laxatives in chronic overdose are known to cause chronic diarrhoea, abdominal pain, hypokalaemia, secondary hyperaldosteronism and renal calculi. Renal tubular damage, metabolic alkalosis and muscle weakness secondary to hypokalaemia have also been described in association with chronic laxative abuse.

Therapy

Drug absorption can be prevented or minimised if short after ingestion vomiting is induced or gastric lavage is made. Replacement of fluids and correction of electrolyte imbalance may be required. This is especially important in the elderly and the young.

Administration of antispasmodics may be of some value.

Recomendations

Inform your doctor or pharmacist of undesirable effects occurred with this drug and which are not described in this package leaflet.

Check the expiry date presented in the this drug package or recipient.

Keep drugs out of the reach of children.

Last revision date of this package leaflet

April 2003

Exhibit F-1

Criteria of Adverse Event Reportability

Exhibit F-1

Expedited reporting of adverse reactions/events

	Occurring in Portugal		Occurring in other Member States		Occurring in non-EU Countries	
	Serious		Serious		Serious	
	Unexpected	Expected	Unexpected	Expected	Unexpected	Expected
Centralized Procedure	+	+	-	-	+	-
Mutual Recognition	+	+	-	-	+	-
National Authorization	+	+	-	-	+	-
Products under Research (clinical trials)	+	+	+	-	+	-
Post-Authorization Safety Studies	+	+	+	-	+	-