GLUCOBAY®

α-Glucosidase inhibitor **Tablets**

Important information, please read carefully!

Composition

1 tablet of Glucobay® 50 contains 50 mg acarbose

Indication

Additional therapy in association with diet in patients with diabetes mellitus.

Impaired glucose tolerance (IGT)*, in combination with diet and exercise.

* defined 2 hour post-glucose load plasma concentration (2HPG) between 7.8 and 11.0 mmol/L (140-200mg/dl) and fasting values between 6.1-6.9 and 7.0 mmol/L (100-125 mg/dL).

Posology and Method of Administration

Dosage Regimen
The dosage must be adjusted by the doctor to suit each patient, because efficacy and tolerability vary from one individual to another.

Unless otherwise prescribed, the recommended dosage is as follows:

Initially	3 x 1 tablet of 50 mg Glucobay/day or
Subsequently	3 x 2 tablets of 50 mg Glucobay/day up to max dose 600 mg / daily (divided into 3 doses)

The dose may be increased after 4 - 8 weeks, and if patients show an inadequate clinical response in the later course of the treatment. If distressing complaints develop in spite of strict adherence to the diet the dose should not be increased further, and if necessary should be somewhat reduced. The average dose is 300 mg Glucobay/day (corresponding to 3 x 2 tablets of Glucobay 50/day).

Elderly (above 65 years): No alteration of dosage or dosing frequency is recommended with regard to the age of the patients.

Children: See contraindications and special warning & precautions for use.

Renal impairment: see contraindications.

Nature and duration of use
Glucobay tablets are effective only if swallowed whole with a little liquid directly before the meal or be chewed with the first few mouthfuls of the meal.

No limit to the length of time for which Glucobay can be used is envisaged.

The limitation on dosage is due to the secondary effects of carbohydrate mal-absorption, in particular distention, flatulence and loose stools. Some adaptation to these effects occurs in the first few weeks of use. The optimal therapeutic dose is established by minimizing whilst reducing postprandial glycaemic rises.

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Contra Indications

Hypersensitivity to acarbose and/or to inactive constituents.
Chronic intestinal disorders associated with distinct disturbances of digestion and absorption.
States which may deteriorate as a result of increased gas formation in the intestine (e.g. Roemheld's syndrome, major hernias, intestinal obstructions, and intestinal ulcers).
Glucobay is contraindicated in-patients with severe renal impairment (creatinine clearance < 25 ml/min).
Inflammatory bowel disease, such as ulcerative colitis and Chron's disease, partial intestinal obstruction or in patients predisposed to intestinal obstruction or ileus.
Since the information on its effects & tolerability in children & adolescents is still insufficient, Glucobay should not be used in patients under 18 years of age
In patients with diabetic ketoacidosis.
In patients with hepatic impairment.

Special Warnings and Precautions For Use

Asymptomatic liver enzyme elevations may occur in individual cases. Therefore, liver enzyme monitoring should be considered during the first 6 to 12 months of treatment. In evaluable cases these changes were reversible on discontinuation of Glucobay therapy.
Safety and efficacy of Glucobay in patients under 18 years of age have not been established.
The administration of antacid preparations containing magnesium and aluminium salts, e.g. hydrotalcite, has been shown not to ameliorate the acute gastrointestinal symptoms of Glucobay in higher dosage and should, therefore, not be recommended to patients for this purpose.

Renal impairment
Plasma concentrations of Glucobay in renally impaired volunteers were proportionally increased relative to the degree of renal dysfunction. Long-term clinical trials in diabetic patients with severe renal dysfunction (creatinine clearance <25 mL/min) have not been conducted. Treatment of patients with severe renal dysfunction (creatinine clearance <25 mL/min) with Glucobay is not recommended.

General
Glucobay delays glucose absorption and lowers hyperglycemia following meals. Regular intake of Glucobay should not be interrupted without the physician's knowledge, since such interruption can cause a rise in blood glucose.

Hepatic impairment
In postmarketing experience with Glucobay, reports of hepatic adverse events have been received , including reports of liver failure, liver transplant, and fulminant hepatitis, with and without fatal outcome. The mechanism is unknown, but Glucobay may contribute to a multifactorial pathophysiology of liver injury, particularly in combination with impaired metabolic control and/or concomitant antidiabetic medications.
Glucobay may give rise to elevations of serum transaminases and, in rare instances, hyperbilirunemia. If elevations are observed, a reduction in dosage or withdrawal of therapy may be indicated, particularly if the elevations persist. Liver enzyme monitoring should be considered during the first 6 to 12 months of treatment.
In patients with a known history of liver impairment or liver disease, liver enzymes should be measured prior to the start of Glucobay therapy and monitored on a regular basis during the first year. If a clinical deterioration or increases in levels of hepatic enzymes are detected, discontinuation of treatment with Glucobay should be considered.

Interaction with Other Medicinal Products and Other Forms of Interactions

Sucrose (cane sugar) and foods containing sucrose often cause abdominal discomfort or even diarrhoea during treatment with Glucobay as a result of increased carbohydrate fermentation in the colon.

Glucobay has an antihyperglycaemic effect, but does not itself induce hypoglycaemia.

If Glucobay is prescribed in addition to drugs containing sulphonylureas or metformin, or in addition to insulin, a fall of the blood glucose values into the hypoglycaemic range may necessitate a suitable decrease in the sulphonylurea, metformin or insulin dose. In individual cases hypoglycaemic shock may occur.

If acute hypoglycaemia develops it should be borne in mind that sucrose (cane sugar) is broken down into fructose and glucose more slowly during treatment with Glucobay; for this reason sucrose is unsuitable for a

rapid alleviation of hypoglycaemia and glucose should be used instead.

In individual cases Glucobay may affect digoxin bioavailability, which may require dose adjustment of digoxin.

Because they may possibly influence the action of Glucobay, simultaneous administration of cholestyramine, intestinal adsorbents, and digestive enzyme products should be avoided. *No interaction was observed with dimeticone/simeticone.*

Certain drugs tend to produce hyperglycaemia and may lead to loss of blood glucose control. These drugs included diuretics (thiazides, furosemide), corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptive, phenytoin, nicotinic acid, symphatomimetics & isoniazid. When such of drugs are administered to a patient receiving acarbose, the patients should be closely monitored for loss of blood glucose control.

Due to neomycin induced mal-absorption of carbohydrate, concomitant administration of neomycin may lead to an enhanced reduction of post prandial blood glucose and to an increased in the frequently and severity of gastrointestinal adverse reactions. If the symptoms are severe, a temporary dose reduction of Glucobay may warranted.

Pregnancy and Lactation

Glucobay should not be administered during pregnancy, as no information is available on its use in pregnant women.

After administration of radio labeled acarbose to lactating rats a small quantity of the radioactivity was found in the milk. There are as yet no corresponding findings in humans. However, as drug-induced effects of acarbose in milk have not been excluded in babies, in principle it is advisable not to prescribe Glucobay during the breast-feeding period.

Undesirable Effects

The frequencies of Adverse Drug Reactions (ADRs) reported with Glucobay based on placebo-controlled studies with Glucobay sorted by CIOMS III categories of frequency (placebo-controlled studies in clinical trial database : Glucobay N = 8.595; placebo N = 7.278; status : 10 Feb 2006) are summarized in the table below.

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Frequencies are defined as very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100) and rare (≥ 1/10,000 to < 1/1,000).

The ADRs identified only during postmarketing surveillance (status: 31 Dec 2005), and for which a frequency could not be estimated, are listed under “not known”

Very Common	Common	Uncommon	Rare	Not known
Blood and Lymphatic System Dsorders				
				Thrombocytopenia
Immune System Disorders				
				Allergic reaction (rash ,erythema, exanthema, urticaria)
Vascular Disorders				
			Oedema	
Gastrointestinal Disorders				
Flatulence	Diarrhea Gastrointestinal and abdominal pains	Nausea Vomiting Dyspepsia		Subileus/ Ileus Pneumatosis cystoidis intestinalis [1]
Hepatobiliary Disorders				

		increase in liver enzymes	Jaundice	Hepatitis

< The MedDRA preferred term is used to describe a certain reaction and its synonyms and related conditions. ADR term representation is based on MedDRA version 11.1. >

In addition events reported as liver disorder, hepatic function abnormal, and liver injury have been received especially from Japan.

Individual cases of fulminant hepatitis with fatal outcome have been reported in Japan. The relationship to Glucobay is unclear.

If the prescribed diabetic diet is not observed the intestinal side effects may be intensified.

If strongly distressing symptoms develop in spite of adherence to the diabetic diet prescribed, the doctor must be consulted and the dose temporarily or permanently reduced.

In patients receiving the recommended daily dose of 150 to 300 mg Glucobay/day, rarely clinically relevant abnormal liver function tests (three times above upper limit of normal range) were observed. (See also section Warnings and Precautions)

Abnormal values may be transient under ongoing acarbose therapy

Postmarket Adverse Drug Reactions
Very rarely (<0.01%), cases of hepatitis, thrombocytopenia and/or jaundice and associated liver damage have been reported. In addition, cases of serum transaminase levels > 10 x ULN have been reported, some of which were associated with jaundice. In most cases where follow-up was reported, hepatic dysfunction improved or resolved upon discontinuation of Glucobay. Reports of liver failure and liver transplant, with and without fatal outcome, have been received. Events reported as liver disorder, hepatic function abnormal, and liver injury have been received, especially from Japan. Individual cases of fulminant hepatitis with fatal outcome have also been reported in Japan. Other, as yet undefined, patient populations may be similarly susceptible.
Very rarely(<0.01%), cases of subileus/ileus, pneumatosis cystoiditis intestinalis, and hypersensitive skin reactions, such as rash, erythema, exanthema and urticaria, have been reported.
Rarely (≥0.01% and <0.1%), edema has been observed.

The majority of adverse experiences reported to Glucobay are gastrointestinal, such as flatulence, diarrhoea and abdominal pain, which result from the pharmacodynamic action of the drug. The majority of symptoms are of mild or moderate intensity and are dose-dependent. In studies of ≥ 6 months duration, the symptoms occurred early (within 1 – 2 months of treatment) and improved tolerability with longer duration of treatment was observed. Failure to adhere to the prescribed diabetic diet, however, can lead to an intensification of these symptoms. Rarely, these gastrointestinal events may be severe and be confused with or due to ileus.

Soft stools are often produced by Glucobay, but if the dosage of the individual case is too high, or after simultaneous ingestion of cane sugar, the stools can become unformed or even liquid. Should diarrhoea persist, patients should be closely monitored and the dosage reduced, or therapy withdrawn, if necessary.

Overdosage

When Glucobay tablets are taken with drinks and/or meals containing carbohydrates (disaccharides, oligosaccharides or polysaccharides), overdosage can lead to meteorism, flatulence and diarrhoea.

In the event of Glucobay tablets being taken in an overdose independently of food, excessive intestinal symptoms need not be anticipated.

In cases of overdosage the patients should not be given drinks or meals containing carbohydrates (disaccharides, oligosaccharides or polysaccharides) for the next 4 to 6 hours.

Properties

PHARMACODYNAMIC PROPERTIES
The active ingredient of Glucobay is acarbose, a pseudotetrasaccharide of microbial origin.

Acarbose exerts its activity in the intestinal tract. The action is based on the inhibition of intestinal enzymes (α-glucosidases) involved in the degradation of disaccharides, oligosaccharides and polysaccharides. This leads to a dose-dependent delay in the digestion of these carbohydrates.

Most importantly, glucose derived from carbohydrates is released and taken up into the blood more slowly. In this way acarbose postpones and reduces the postprandial rise in blood glucose. As a result of the balancing effect on the uptake of glucose from the intestine, the blood glucose fluctuations over the day are reduced and the mean blood glucose values decrease.

PHARMACOKINETICS PROPERTIES
The bioavailabitily is 1-2% only. This extremely low systemically available percentage of inhibitory substance is desirable, because acarbose acts only locally in the intestine. Thus, this low bioavailability has no relevance for the therapeutic effect.

Presentations

Glucobay 50 : Box of 5 blisters @ 10 tablets; Reg. No. XXXXXXXXXXXXXX

Storage

Store below 30ºC

Keep drugs out of reach of children.

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Harus dengan resep dokter