Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Diastabol 100 mg tablet.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Diastabol 100 mg tablet contains miglitol 100 mg.

For excipients see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White to slightly pale yellow, round, biconvex tablet.

Diastabol 100 mg tablets are blank on one side and imprinted with ‘MIG 100’ on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Diastabol is recommended as an adjunct to diet or diet and sulfonylureas for the treatment of non-insulin-dependent diabetes mellitus (NIDDM) in patients inadequately controlled on diet alone, or on diet and sulfonylureas.

4.2 Posology and method of administration

Diastabol tablets are taken orally and should be chewed with the first mouthful of food, or swallowed whole with a little liquid directly before the meal.

Adults
The recommended initial dose is 50 mg three times a day. Depending upon tolerability, the dose should normally be increased to the recommended maintenance dose of 100 mg three times a day after four or twelve weeks’ treatment.

Elderly patients
No modification of the normal adult dosage regimen is necessary.

Hepatic impairment
No dosage adjustment is necessary.

Renal impairment
No dosage adjustment is necessary for patients with mild to moderate renal insufficiency (creatinine clearance > 25 ml/min).

4.3 Contraindications

- Hypersensitivity to miglitol or to any of the excipients.
- Miglitol should not be used in children and individuals less than 18 years of age.
- Breast-feeding woman.
- Patients with inflammatory bowel disease, colonic ulceration, partial intestinal obstruction or patients predisposed to intestinal obstruction. In addition, miglitol should not be used in patients who have chronic intestinal diseases associated with marked disorders of digestion or absorption and patients who suffer from states which may deteriorate as a result of increased gas formation in the intestine (e.g. larger hernias).
- As miglitol clearance has shown to be reduced with impaired renal function and its effects have not been fully evaluated in patients with marked renal impairment, its use is contra-indicated in patients with a creatinine clearance of less than 25 ml/min.

4.4 Special warnings and precautions for use

Hypoglycaemia

Miglitol may act to potentate the hypoglycaemic effects of sulfonylureas, and the dosages of these agents may need to be adjusted accordingly. However, this effect has not been seen in clinical trials with miglitol. Hypoglycaemic episodes occurred in clinical trials in combination with insulin. Episodes of hypoglycaemia occurring during therapy must, where appropriate, be treated by the administration of glucose, not sucrose. This is because miglitol delays the absorption of disaccharides, but not monosaccharides.

4.5 Interaction with other medicinal products and other forms of interaction

The bioavailability of glibenclamide and metformin is slightly reduced when administered concomitantly with miglitol, but the results of clinical trials with these combinations indicate that any pharmacokinetic interaction between these agents is unlikely to be of clinical relevance.

Intestinal adsorbents (e.g. charcoal) and digestive enzyme preparations containing carbohydrate-splitting enzymes (e.g. amylase, pancreatin) may reduce the effect of miglitol and therefore should not be taken concomitantly.

Since miglitol may lead to gastro-intestinal symptoms including soft stools and diarrhoea, the effects of laxatives may be enhanced. As with other causes of diarrhoea, the potential effects on concomitant medicinal products, particularly sustained release preparations, should also be considered owing to the possibility of altered gastro-intestinal transit times.

As miglitol administration may lead to reduced absorption of propranolol, dose adjustment of these compounds may be necessary when they are given in combination with miglitol. However, regarding propranolol, no modification of hemodynamic parameters was seen in pharmacological studies. Concomitant administration of miglitol and digoxin to non-patients volunteers has resulted in a reduction in digoxin plasma concentrations. However, this effect was not observed in NIDDM patients pre-treated for at least four weeks with digoxin. This pharmacokinetic interaction may therefore be of no clinical relevance.

No interaction was observed between miglitol and nifedipine, or between miglitol and antacids consisting of magnesium hydroxide and aluminium hydroxide.

4.6 Fertility, pregnancy and lactation

Pregnancy

No data concerning the use of miglitol during pregnancy in humans is available. Animal studies do not indicate harmful effects with respect to pregnancy, embryonal or fœtal development, parturition or postnatal development.

When the patient plans to become pregnant and during pregnancy, diabetes should not be treated with miglitol but insulin should be used to maintain blood glucose levels as close to normal as possible in order to lower risk of fœtal malformations associated with abnormal blood glucose levels.

Lactation

Miglitol must not be used during lactation (See 4.3). Miglitol is excreted in milk in very low concentrations.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

Patients should be alerted to the possible risk of hypoglycaemia when miglitol is used in combination with a sulfonylurea.

4.8 Undesirable effects

The frequencies listed below are defined as: very common (≥1/10), common (≥1/100 to <1/10) and uncommon (≥1/1,000 to <1/100).

Metabolism and nutrition disorders
When used in combination with other anti-diabetic treatments (sulfonylureas and insulin), hypoglycaemia has been commonly reported (See 4.4).

Gastrointestinal disorders
Owing to its mode of action, miglitol may result in a greater proportion of undigested carbohydrate being digested in the large bowel. These carbohydrates may also be utilised by the intestinal flora, resulting in the increased formation of intestinal gas. The majority of patients are therefore likely to experience one or more gastro-intestinal symptoms:

Very common: flatulence, diarrhoea and abdominal pain.
Common: nausea, constipation and dyspepsia.

The symptoms are related to both dose and dietary substrate and may subside with continued treatment. Symptoms can be reduced by adherence to the prescribed diabetic diet and the avoidance of sucrose, or foodstuffs containing sugar. If symptoms are poorly tolerated, a reduction in dosage is recommended.

Should diarrhoea persist, patients should be closely monitored and the dosage reduced or therapy withdrawn, if necessary.

Common: transaminases increased.
Uncommon: hepatic function abnormal

4.9 Overdose

No case of overdose has been reported. No specific antidotes to miglitol are known. In the event of overdosing, patients are likely to suffer from gastro-intestinal symptoms, for example, flatulence, diarrhoea and abdominal pain. Abdominal distension, softer stools, borborygmi (meteorism) and a feeling of fullness may also occur.

Intake of carbohydrate-containing meals or beverages should be avoided for 4-6 hours.

Diarrhoea should be treated by standard conservative measures. Further treatment is supportive and symptomatic.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Alpha-Glucosidase Inhibitor

ATC code: A10B F02

Miglitol is a reversible inhibitor of intestinal alpha-glucosidases. Under the influence of miglitol, the digestion of complex carbohydrates into absorbable monosaccharides in the small intestine is dose-dependently delayed. Administration of miglitol thus leads to reduced postprandial hyperglycaemia and a smoothing effect on fluctuations in the daily blood glucose profile. The absorption of orally administered glucose is not inhibited by miglitol.

In contrast to sulfonylureas miglitol does not stimulate pancreatic insulin secretion.

Treatment with miglitol also results in a reduction of fasting blood glucose and to changes in levels of glycosylated haemoglobin (HbA1, HbA1c). The changes may be a reduction or reduced deterioration in HbA1 or HbA1c levels, depending upon the patient's clinical status and disease progression. These parameters are affected in a dose-dependent manner by miglitol.

5.2 Pharmacokinetic properties

The pharmacodynamic action of miglitol is local in the gastro-intestinal tract.

Following oral administration of low doses of miglitol (12.5 to 25mg), the compound is almost quantitatively absorbed. Increasing the oral dose of miglitol from 25 to 200 mg resulted in non-linear changes in its absorption. Within the recommended dosage range, approximately 90 % of a 50 mg dose is absorbed in comparison to 60 % of a 100 mg dose. The absorption characteristics of miglitol follow Michaelis-Menten kinetics with an absorption window of 6-10 hours following administration. Its steady-state volume of distribution (Vss) of 0.18 l/kg indicates that miglitol is distributed principally in the extracellular space. Miglitol is bound to plasma proteins only in negligible quantities (< 4 %).

The drug is not metabolised in the gut or after absorption, but is eliminated unchanged almost exclusively via the kidneys. Miglitol clearance may be reduced in patients with impaired renal function. The biliary excretion of miglitol is negligible (<1%). The total body clearance is therefore equal to the renal clearance (99 to 114 ml/min in young non-patient volunteers), and corresponds to the glomerular filtration rate. The apparent terminal half-life, t1/2, in the majority of young non-patient volunteers is in the range of 2-3 hours.

5.3 Preclinical safety data

In chronic toxicity studies weight loss was the dose-limiting toxicity. Specific target organs for toxicity could not be determined.

Miglitol had no genotoxic potential in a battery of genotoxicity tests, and there was no sign of miglitol-induced carcinogenicity in mice and rats.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Magnesium stearate
Maize starch

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

No special precaution for storage.

6.5 Nature and contents of container

Blister strips in hard cardboard outers comprising:

Polypropylene foil (colourless) sealed with aluminium foil
PVC/PVDC foil (colourless) and aluminium foil
Polyamide/aluminium/PVC foil and aluminium foil

Pack sizes: 15, 20, 30, 50, 60, 90, 120, 240 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

sanofi-aventis Ireland Limited
Citywest Business Campus
Dublin 24

8 MARKETING AUTHORISATION NUMBER

PA 0540/144/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 4th April 1997

Date of last renewal: 23rd July 2006

10 DATE OF REVISION OF THE TEXT

March 2011