Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Acarbose Tecnimede 50 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg of Acarbose.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White, circular, plain tablets, scored on one side.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Acarbose is recommended for the treatment of type II diabetes mellitus in patients inadequately controlled on diet alone, or on diet and oral hypoglycaemic agents.

4.2 Posology and method of administration

Acarbose 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. Owing to the great individual variation of glucosidase activity in the intestinal mucosa, there is no fixed dosage regimen, and patients should be treated according to clinical response and tolerance of intestinal side effects.

Adults
The recommended initial dose is 50 mg three times a day. However, some patients may benefit from more gradual initial dose titration to minimise gastrointestinal side effects. This may be achieved by initiating treatment at 50 mg once or twice a day, with subsequent titration to a three times a day regimen.

If after six to eight weeks' treatment patients show an inadequate clinical response, the dosage may be increased to 100 mg three times a day. A further increase in dosage to a maximum of 200 mg three times a day may occasionally be necessary.

Patients receiving the maximum dose
require careful monitoring (see Special warnings and precautions for use, Section 4.4).

Acarbose is intended for continuous long-term treatment.

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

Children and adolescents under 18 years

The efficacy and safety of acarbose in children and adolescents have not been established. Acarbose is not recommended for patients under the age of 18 years.

Renal or hepatic impairment
See section 4.3.

4.3 Contraindications

Hypersensitivity to acarbose or any of the excipients. Acarbose is also contra-indicated in patients with inflammatory bowel disease, colonic ulceration, partial intestinal obstruction or in patients predisposed to intestinal obstruction. In addition, should not be used in patients who have chronic intestinal diseases associated with marked disorders of digestion or absorption and in patients who suffer from states which may deteriorate as a result of increased gas formation in the intestine, e.g. larger hernias.

Acarbose is contra-indicated in patients with hepatic impairment
As Acarbose has not been studied in patients with severe renal impairment, it should not be used in patients with a creatinine clearance < 25 ml/min/1.73m².

4.4 Special warnings and precautions for use

Hypoglycaemia: When administered alone, Acarbose does not cause hypoglycaemia. It may, however, act to potentiate the hypoglycaemic effects of insulin and sulphonylurea drugs, and the dosages of these agents may need to be modified accordingly. In individual cases hypoglycaemic shock may occur (i.e. clinical sequelae of glucose levels < 1 mmol/L such as altered conscious levels, confusion or convulsions).

Episodes of hypoglycaemia occurring during therapy must, where appropriate, be treated by the administration of glucose, not sucrose. This is because acarbose will delay the digestion and absorption of disaccharides, but not monosaccharides.

Transaminases: Patients treated with acarbose may, on rare occasions, experience an idiosyncratic response with either symptomatic or asymptomatic hepatic dysfunction. In the majority of cases this dysfunction is reversible on discontinuation of acarbose therapy. It is recommended that liver enzyme monitoring is considered during the first six to twelve months of treatment. If elevated transaminases are observed, withdrawal of therapy may be warranted, particularly if the elevations persist. In such circumstances, patients should be monitored at weekly intervals until normal values are 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 Acarbose in higher dosage and should, therefore, not be recommended to patients for this purpose.

4.5 Interaction with other medicinal products and other forms of interaction

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

The concomitant administration of neomycin may lead to enhanced reductions of postprandial blood glucose and to an increase in the frequency and severity of gastro-intestinal side effects. If the symptoms are severe, a temporary dose reduction of Acarbose may be warranted.

The concomitant administration of colestyramine may enhance the effects of Acarbose, particularly with respect to reducing postprandial insulin levels. Simultaneous administration of Acarbose and colestyramine should, therefore, be avoided. In the rare circumstance that both Acarbose and colestyramine therapy are withdrawn simultaneously, care is needed as a rebound phenomenon has been observed with respect to insulin levels in non-diabetic subjects.

In individual cases Acarbose may affect digoxin bioavailability, which may require dose adjustment of digoxin. Monitoring of serum digoxin levels should be considered.

In a pilot study to investigate a possible interaction between Acarbose and nifedipine, no significant or reproducible changes were observed in the plasma nifedipine profiles.

4.6 Fertility, pregnancy and lactation

Pregnancy
For acarbose, no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/ foetal development, parturition or postnatal development (see section 5.3).

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

Lactation
It is unknown whether acarbose is excreted in human breast milk. Animal studies have shown excretion of acarbose in breast milk. Acarbose should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

Acarbose monotherapy does not cause hypoglycaemia and is therefore unlikely to have effects on the ability to drive or to use machines. However, patients should be alerted to the risk of hypoglycaemia when acarbose is used in combination with other antidiabetic agents.

4.8 Undesirable effects

Adverse drug reactions (ADRs) based on placebo-controlled studies with acarbose sorted by CIOMS III categories of frequency (placebo-controlled studies in clinical trial database: acarbose N = 8,595; placebo N = 7,278; status: 10 Feb 2006) are listed below.
ADRs derived from post marketing reports (status: 31 Dec 2005) are printed in *italic.*

System Organ Class	**Very Common (≥ 1/10)**	**Common (≥ 1/100, < 1/10)**	**Uncommon (≥ 1/1000, < 1/100)**	**Rare (≥ 1/10,000, < 1/1000)**	**Very Rare (< 1/10,000)**
Blood and the lymphatic system disorders					*Thrombocytopenia*
Gastrointestinal disorders (1)	Flatulence Borborygmi Abdominal distension	Diarrhoea Abdominal pain	Nausea Vomiting		*Ileus* *Subileus* *Constipation*
Hepatobiliary disorders (2)				Liver enzyme	*Hepatitis*

				increase	*Jaundice*
Skin and subcutaneous tissue disorders					*Hypersensitivity skin reactions (Rash, Erythema, Exanthema,Urticaria) Oedema*

(1) Diarrhoea and abdominal pain may occur after sucrose-containing foods are ingested. If the prescribed diabetic diet is not observed the gastrointestinal adverse events may be intensified. The symptoms are related both to the dose and to the dietary substrate and may diminish with continued treatment. If severe symptoms develop in spite of adherence to the prescribed diabetic diet the dose must be temporarily or permanently reduced. Often the dose reduction is sufficient for one of the main meals (lunch or dinner). Should diarrhoea persist, then patients should be closely monitored and the dosage reduced or therapy withdrawn, if necessary.

(2) Rarely, clinically significant abnormal hepatic function tests (three times above the upper limit for normal values) have been observed in patients treated with the recommended daily dose of 150mg to 300mg of acarbose daily. Abnormal values may be temporary during treatment (see section 4.4).

If ileus or subileus is suspected, treatment must be stopped immediately. In Japan, individual cases of fulminant liver failure have been observed, although the role of acarbose is unclear.

Individual cases of fulminant hepatitis with fatal outcome have been reported in Japan. The relationship to acarbose 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 Acarbose, clinically relevant abnormal liver function tests (three times above upper limit of normal range) were rarely observed. Abnormal values may be transient under ongoing Acarbose therapy. (See Section 4.4).

4.9 Overdose

When Acarbose tablets are taken with drinks and/or meals containing carbohydrates overdose may lead to meteorism, flatulence and diarrhoea. If Acarbose tablets are taken independently of food, excessive intestinal symptoms need not be anticipated.

No specific antidotes to Acarbose are known.
Intake of carbohydrate-containing meals or beverages should be avoided for 4-6 hours.

Diarrhoea should be treated by standard conservative measures.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Alpha glucosidase inhibitors, ATC code: A10B F01.

In all species tested, acarbose exerts its activity in the intestinal tract. The action of acarbose is based on the competitive 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. Glucose derived from these carbohydrates is released and taken up into the blood more slowly. In this way, acarbose reduces the postprandial rise in blood glucose, thus reducing blood glucose fluctuations.

5.2 Pharmacokinetic properties

Following administration, only 1-2% of the active inhibitor is absorbed.

The pharmacokinetics of Acarbose were investigated after oral administration of the ^{14}C-labelled substance (200 mg) to healthy volunteers. On average, 35 % of the total radioactivity (sum of the inhibitory substance and any degradation products) was excreted by the kidneys within 96 h. The proportion of inhibitory substance excreted in the urine was 1.7 % of the administered dose. 50 % of the activity was eliminated within 96 hours in the faeces. The course of the total radioactivity concentration in plasma was comprised of two peaks. The first peak, with an average acarbose-equivalent concentration of 52.2 ± 15.7 µg/l after 1.1 ± 0.3 h, is in agreement with corresponding data for the concentration course of the inhibitor substance (49.5 ± 26.9 µg/l after 2.1 ± 1.6 h). The second peak is on average 586.3 ± 282.7 µg/l and is reached after 20.7 ± 5.2 h. The second, higher peak is due to the absorption of bacterial degradation products from distal parts of the intestine. In contrast to the total radioactivity, the maximum plasma concentrations of the inhibitory substance are lower by a factor of 10-20. The plasma elimination half-lives of the inhibitory substance are 3.7 ± 2.7 h for the distribution phase and 9.6 ± 4.4 h for the elimination phase.

A relative volume of distribution of 0.32 l/kg body-weight has been calculated in healthy volunteers from the concentration course in the plasma.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose

Colloidal anhydrous silica

Magnesium stearate

Pregelatinised starch

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 30° C. Store in the original packaging to protect from light and moisture.

6.5 Nature and contents of container

Transparent and colourless PVC/PCTFE/PVC film/Al foil blisters, packed in outer cartons is used as container closure system for Acarbose tablets.

Pack sizes: 10, 20, 30, 40, 50, 60, 90, 120 and 270 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Multigeneris GmbH
Marlowring 21
22525 Hamburg
Germany

8 MARKETING AUTHORISATION NUMBER

PA 1773/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29 January 2010

10 DATE OF REVISION OF THE TEXT

September 2013