Public Assessment Report

Decentralised Procedure

ACARBOSE 50MG TABLETS
ACARBOSE 100MG TABLETS

(Acarbose)

Procedure No: UK/H/1362/001-2/DC

UK Licence No: PL 00289/1114-5

TEVA UK LIMITED
LAY SUMMARY

On 08 June 2011, Germany, France, Hungary, Poland, Portugal and the UK agreed to grant Marketing Authorisations to Teva UK Limited for the medicinal products Acarbose 50mg and 100mg tablets (PL 00289/1114-5; UK/H/1362/001-2/DC) via the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS). After a subsequent national phase, Marketing Authorisations were granted in the UK on 28 June 2011.

These are prescription-only medicines (POM) used in the management of Type II diabetes. If you have Type II diabetes then levels of sugar (glucose) in your blood are too high. This medicine works by slowing down digestion and absorption of sugars from your diet and stops levels of blood sugar from rising too high. This medicine can be used alone or in combination with a sulphonylurea and/or metformin.

Acarbose 50mg and 100mg tablets contains the active ingredient acarbose, which belongs to a class of medicines called “alpha glucosidase inhibitors”.

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Acarbose 50mg and 100mg tablets outweigh the risks, hence Marketing Authorisations have been granted.
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## Module 1

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<td><strong>Strength</strong></td>
<td>50mg and 100mg</td>
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<tr>
<td><strong>MA Holder</strong></td>
<td>Teva UK Limited, Brampton Road, Hampden Park, Eastbourne, BN22 9AG, UK.</td>
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<td><strong>Reference Member State (RMS)</strong></td>
<td>UK</td>
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Module 2

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT
Acarbose 50mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 50mg Acarbose.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Tablet.

Acarbose 50mg tablets are round, biconvex, white to off-white tablets, with bossing "ACA 50" on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Acarbose is recommended for the treatment of non-insulin dependent (NIDDM) diabetes mellitus in patients inadequately controlled on diet alone, or on diet and (i) metformin and / or (ii) a sulphonylurea.

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 50mg 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 50mg 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 100mg three times a day. A further increase in dosage to a maximum of 200mg three times a day may occasionally be necessary.

Acarbose is intended for continuous long-term treatment.

If adverse events occur in spite of strict adherence to the diabetic diet, the dose should not be increased and if necessary should be reduced (see section 4.8).

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 contraindicated in patients with inflammatory bowel disease, colonic ulceration, partial intestinal obstruction or in patients predisposed to intestinal obstruction. In addition, Acarbose 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 contraindicated 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.

If ileus or sub-ileus is suspected, treatment must be stopped immediately (see section 4.8).

It is essential to adhere to a strict diabetic diet when taking Acarbose.

Regular use of Acarbose should not be interrupted without medical advice as this may lead to a rise in blood glucose.

Since the information available on its effects and tolerability in children and adolescents is still insufficient, Acarbose should not be used in patients under 18 years of age.

4.5 Interaction with other medicinal products and other forms of interaction

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

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.

Several therapeutic agents including thiazide and other diuretics, corticosteroids, phenothiazines, thyroid hormones, oestrogens and oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blockers and isoniazid can cause hyperglycaemia, which may attenuate the pharmacodynamic effects of Acarbose. Blood glucose levels should be closely monitored if any of
these agents are used by patients receiving Acarbose, or if treatment with Acarbose is contemplated in patients already receiving any of these agents.

If Acarbose is prescribed in addition to other oral hypoglycaemic agents (e.g. a sulphonylurea or metformin), a fall of the blood glucose into the hypoglycaemic range may necessitate a decrease in the dose of the concomitant medication.

4.6 Pregnancy and lactation

Pregnancy
The safety of this medicinal product for use in human pregnancy has not been established. An evaluation of experimental animal studies does not indicate direct or indirect harmful effects with respect to reproduction, development of the embryo or fetus, the course of gestation, and peri- and postnatal development.

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 fetal 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 metformin and / or a sulphonylurea.

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.

Frequencies are defined as very common (≥1/10); common (>1/100 to <1/10); uncommon (>1/1000 to <1/100); rare (>1/10000 to <1/1000); very rare (<1/10 000).

Blood and the lymphatic system disorders:
Not known (cannot be estimated from the available data): Thrombo-cytopenia*

Immune System Disorders:
Not known (cannot be estimated from the available data): Allergic reaction (rash, erythema, exanthema, urticaria)*

Vascular Disorders:
Rare: Oedema

Gastrointestinal Disorders:
Very common: Flatulence
Common: Diarrhoea, Gastrointestinal and abdominal pains
Uncommon: Nausea, Vomiting, Dyspepsia
Not known (cannot be estimated from the available data): Subileus/ileus, Pneumatosis cystoides intestinalis*

Hepatobiliary Disorders:
Uncommon: Transient increase in liver enzymes
Rare: Jaundice
Not known (cannot be estimated from the available data): Hepatitis*

*ADRs derived from post marketing reports (status: 31 Dec 2005).

If ileus or subileus is suspected, treatment must be stopped immediately. 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: A10BF01

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.

In contrast to sulphonylureas acarbose has no stimulatory action on the pancreas.

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

5.2 Pharmacokinetic properties
Following oral administration, only 1-2% of the active inhibitor is absorbed.

The pharmacokinetics of acarbose were investigated after oral administration of the 14C-labelled substance (200mg) 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.

A markedly reduced body weight gain in rats and dogs after repeated administration of acarbose was considered as pharmacodynamic effect (loss of carbohydrates) and could be counteracted by increase of food or glucose supplementation.

Carcinogenicity was studied in Sprague-Dawley rats, Wistar rats and hamsters. An increased tumour incidence in certain tissues (kidney, testis) was observed if malnutrition due to acarbose was not corrected. No increase in tumour rate was observed if the body weight gain was kept normal by food or glucose supplementation.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Cellulose, microcrystalline
Starch pregelatinized, maize
Silica, colloidal anhydrous
Magnesium stearate

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Do not store above 25 °C. Store in the original packaging in order to protect from moisture.

6.5 Nature and contents of container
20, 21, 30, 40, 50, 60, 90, 100, 105, 120, 270 tablets in PVC/PE/PVDC aluminium blisters. 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 AUTHORITY
Teva UK Limited
Brampton Road
Hampden Park
Eastbourne
BN22 9AG
United Kingdom

8 MARKETING AUTHORITY NUMBER(S)
PL 00289/1114

9 DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION
28/06/2011

10 DATE OF REVISION OF THE TEXT
28/06/2011
1 NAME OF THE MEDICINAL PRODUCT
Acarbose 100mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 100mg Acarbose.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Tablet.

Acarbose 100mg tablets are round, biconvex, white to off-white tablets, with a score-line on one side and bossing “ACA 100” on the other side. The scoreline 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 non-insulin dependent (NIDDM) diabetes mellitus in patients inadequately controlled on diet alone, or on diet and (i) metformin and / or (ii) a sulphonylurea.

4.2 Posology and method of administration
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Adults
The recommended initial dose is 50mg 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 50mg 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 100mg three times a day. A further increase in dosage to a maximum of 200mg three times a day may occasionally be necessary.

Acarbose is intended for continuous long-term treatment.

If adverse events occur in spite of strict adherence to the diabetic diet, the dose should not be increased and if necessary should be reduced (see section 4.8).

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 contraindicated in patients with inflammatory bowel disease, colonic ulceration, partial intestinal obstruction or in patients predisposed to intestinal obstruction. In addition, Acarbose 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 contraindicated 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.
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**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.

If ileus or sub-ileus is suspected, treatment must be stopped immediately (see section 4.8).

It is essential to adhere to a strict diabetic diet when taking Acarbose.

Regular use of Acarbose should not be interrupted without medical advice as this may lead to a rise in blood glucose.

Since the information available on its effects and tolerability in children and adolescents is still insufficient, Acarbose should not be used in patients under 18 years of age.

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

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.

Several therapeutic agents including thiazide and other diuretics, corticosteroids, phenothiazines, thyroid hormones, oestrogens and oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blockers and isoniazid can cause hyperglycaemia, which may attenuate the pharmacodynamic effects of Acarbose. Blood glucose levels should be closely monitored if any of these agents are used by patients receiving Acarbose, or if treatment with Acarbose is contemplated in patients already receiving any of these agents.

If Acarbose is prescribed in addition to other oral hypoglycaemic agents (e.g. a sulphonylurea or
metformin), a fall of the blood glucose into the hypoglycaemic range may necessitate a decrease in the dose of the concomitant medication.

4.6 Pregnancy and lactation

Pregnancy

The safety of this medicinal product for use in human pregnancy has not been established. An evaluation of experimental animal studies does not indicate direct or indirect harmful effects with respect to reproduction, development of the embryo or fetus, the course of gestation, and peri- and postnatal development.

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 fetal 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 metformin and / or a sulphonylurea.

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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.

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Not known (cannot be estimated from the available data): Thrombo-cytopenia*

Immune System Disorders:
Not known (cannot be estimated from the available data): Allergic reaction (rash, erythema, exanthema, urticaria)*

Vascular Disorders:
Rare: Oedema

Gastrointestinal Disorders:
Very common: Flatulence
Common: Diarrhoea, Gastrointestinal and abdominal pains
Uncommon: Nausea, Vomiting, Dyspepsia
Not known (cannot be estimated from the available data): Subileus/ileus, Pneumatosis cystoides intestinalis*

Hepatobiliary Disorders:
Uncommon: Transient increase in liver enzymes
Rare: Jaundice
Not known (cannot be estimated from the available data): Hepatitis*

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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: A10BF01

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
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In contrast to sulphonylureas acarbose has no stimulatory action on the pancreas.

Treatment with acarbose also results in a reduction of fasting blood glucose and to modest changes in
levels of glycated 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 acarbose.

5.2 Pharmacokinetic properties

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

The pharmacokinetics of acarbose were investigated after oral administration of the ^14C-labelled
substance (200mg) 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 ± 15.7μg/l after 1.1 ± 0.3 h, is in agreement with corresponding data
for the concentration course of the inhibitor substance (49.5 ± 26.9μg/l after 2.1 ± 1.6 h). The second
peak is on average 586.3 ± 282.7μg/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.

A markedly reduced body weight gain in rats and dogs after repeated administration of acarbose was
considered as pharmacodynamic effect (loss of carbohydrates) and could be counteracted by increase
Carcinogenicity was studied in Sprague-Dawley rats, Wistar rats and hamsters. An increased tumour incidence in certain tissues (kidney, testis) was observed if malnutrition due to acarbose was not corrected. No increase in tumour rate was observed if the body weight gain was kept normal by food or glucose supplementation.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Cellulose, microcrystalline
Starch pregelatinized, maize
Silica, colloidal anhydrous
Magnesium stearate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Do not store above 25 °C. Store in the original packaging in order to protect from moisture.

6.5 Nature and contents of container
20, 21, 30, 40, 50, 60, 90, 100, 105, 120, 270 tablets in PVC/PE/PVDC aluminium blisters. 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
Teva UK Limited
Brampton Road
Hampden Park
Eastbourne
BN22 9AG
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
PL 00289/1115

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
28/06/2011

10 DATE OF REVISION OF THE TEXT
28/06/2011
ACARBOSE 60 mg TABLETS,  
ACARBOSE 100 mg TABLETS  
(acarbose)

PACKAGE LEAFLET: INFORMATION FOR THE USER

Read all of this leaflet carefully before you start taking this medicine.
• Keep this leaflet. You may need to read it again.
• If you have any further questions, ask your doctor or pharmacist.
• This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
• If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

IN THIS LEAFLET:
1. What Acarbose tablets are and what they are used for
2. Before you take Acarbose tablets
3. How to take Acarbose tablets
4. Possible side effects
5. How to store Acarbose tablets
6. Further information

1 WHAT ACARBOSE TABLETS ARE AND WHAT THEY ARE USED FOR

Your medicine belongs to a class of medicines called “Alpha glucosidase inhibitors” and is used in the management of Type II diabetes (diabetes that does not require treatment with insulin injections). It can be used alone or in combination with a sulphonylurea and/or metformin. If you have Type II diabetes then levels of sugar (glucose) in your blood are too high. Your medicine works by slowing down digestion and absorption of sugars from your diet. This stops levels of blood sugar from rising too high.

During treatment you should also ensure that you follow the diet recommended by your doctor.

2 BEFORE YOU TAKE ACARBOSE TABLETS

Do NOT take ACARBOSE TABLETS:
• If you are allergic (hypersensitive) to acarbose (the active ingredient in your medicine) or to any of the other ingredients.
• If you have inflammatory bowel disease.
• If you suffer from ulcers in your colon – e.g. Crohn’s Disease or Ulcerative colitis. Ask your doctor if unsure.
• If you have or have previously suffered from an obstruction in your intestines (gut). Ask your doctor if unsure.
• If you have any condition which may be made worse by the formation of gas in your intestines. For example, if you have a large hernia. Ask your doctor if unsure.
• If you have severe kidney problems.

Take special care with Acarbose tablets

You may experience low blood sugar levels if you take other anti-diabetic agents at the same time as acarbose, such as sulphonylureas or insulin. Tell your doctor if you are already taking medicines for the treatment of your diabetes. Low blood sugar levels can cause some of the following symptoms:
• double vision
• confusion
• slurred speech
• faintness
• trembling
• palpitations (abnormal awareness of your own heartbeat).

Low blood sugar is a potentially serious condition. If you experience any of the above symptoms then take some glucose to increase your levels of blood sugar back to normal. You will be able to buy glucose tablets, syrup or sweets at your local pharmacy. It is a good idea to carry some glucose with you at all times in case you need to use it. Other sugars such as sucrose (table sugar) will not work because Acarbose tablets prevents them from being absorbed. If you have experienced the above symptoms then you should make an appointment to see your doctor for your medication to be reviewed.

Your doctor may decide to conduct blood tests to monitor your liver during treatment with Acarbose tablets, particularly during the first 8 to 12 months of treatment.

Taking other medicines

Talk to your doctor if you are taking any of the following:
• charcoal (used for treatment of poisoning or drug overdose)
• digestive enzyme preparations (e.g. pancreatin and amylase)
• neomycin (antibiotic used before bowel surgery)
• coenzyme Q10 (used for treating weakness resulting from liver problems, high cholesterol or diarrhoea)
• digoxin (used for treatment of heart failure or heart rhythm problems)
• thiazides or calcium channel blockers (used in the treatment of high blood pressure)
• corticosteroids (used to treat inflammation)
• phenoxytoin (used to treat epilepsy fits)
• phenothiazine (used to treat mental health)
• thyroid medicines
• female sex hormone (oestrogen), oral contraceptives
• nicotinic acid (used to lower blood cholesterol)
• medicines called “sympathomimetics” such as ephedrine and norepinephrine: these may be used in the treatment of cardiac arrest, severe drop in blood pressure or premature labour
• isoniazid (used to treat tuberculosis).

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Taking Acarbose tablets with food and drink

Your tablets should be swallowed whole immediately before a meal or chewed with the first mouthful of food. Your tablets should not be taken between meals.

Sucrose (cane sugar) and foods containing sucrose can cause abdominal discomfort or even diarrhoea due to carbohydrate-fermentation in the colon during treatment with Acarbose tablets.

Pregnancy and breast-feeding

Acarbose tablets are not recommended for use during pregnancy or breast-feeding as the effects on your baby are not known. If you are planning to become pregnant, or are already pregnant or breast-feeding, you should speak to your doctor before taking Acarbose tablets.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Acarbose tablets do not affect your ability to drive or operate machinery if taken on their own. However, you may experience low blood sugar levels if you take other anti-diabetic agents at the same time, such as sulphonylureas or metformin. This may affect your ability to drive or operate machinery safely.
PAR Acarbose 50mg and 100mg tablets

HOW TO TAKE ACARBOSE TABLETS

Always take Acarbose tablets exactly as your doctor has told you to. You should check with your doctor or pharmacist if you are not sure.

Adults and elderly patients

The usual dose is 50 mg three times a day before meals. However, your doctor may start you on a lower dose (e.g. 50 mg once or twice a day) and increase your dose slowly to reduce the risk of side effects occurring.

If you require a larger dose your doctor may decide to increase your dose further to 100 mg three times a day. Occasionally it may be necessary to increase the dose to 200 mg three times a day.

Acarbose tablets should be swallowed whole immediately before meals or chewed with the first mouthful of food.

Children and adolescents under 18 years

Use of Acarbose tablets is not recommended.

If you take more Acarbose tablets than you should

If you (or someone else) swallow a lot of the tablets all together, or if you think a child has swallowed any of the tablets, contact your nearest hospital casualty department or your doctor immediately. You should also not consume any carbohydrate containing food or drink. An overdose is likely to cause a swollen abdomen (resulting from the presence of excessive amounts of gas), flatulence (wind) and diarrhoea. Please take this leaflet, any remaining tablets and the container with you to the hospital or doctor so that they know which tablets were consumed.

If you forget to take Acarbose tablets

If you forget to take a dose of your medicine then do not take the missed dose between meals. Wait until your next scheduled dose and meal and continue taking your tablets as per normal. Do not take a double dose to make up for a forgotten tablet.

If you stop taking Acarbose tablets

It is important to keep taking Acarbose tablets according to your doctor’s instructions to ensure that levels of blood sugars do not rise to high. Do not stop taking Acarbose tablets without discussing it with your doctor first.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

POSSIBLE SIDE EFFECTS

Like all medicines, Acarbose tablets can cause side effects, although not everybody gets them. Some of the side effects are serious. The frequencies of the following side effects are unknown. However, if you suffer from any of these reactions you should seek urgent medical attention:

- Bleeding or bruising more easily than normal (caused by a reduction in blood platelets)
- Allergic reaction (rash, redness of the skin, skin eruptions, nettle rash)
- Partial or complete obstruction of the intestine leading to pain and vomiting
- Inflammation of the liver (may cause abdominal discomfort, jaundice, loss of appetite).

The following side effects have also been reported:

Very common (affects more than 1 user in 10):
- Flatulence (wind).

Common (affects 1 to 10 users in 100):
- Diarrhoea
- Pain in the stomach or abdomen.

Uncommon (affects 1 to 10 users in 1,000):
- Nausea
- Vomiting
- Indigestion
- Increase in liver enzymes, which may cause a change in blood test results that report on how the liver is working.

Rare (affects 1 to 10 users in 10,000):
- Fluid retention causing swelling of arms and legs
- Jaundice (yellowing of the skin and whites of the eyes).

Other possible side effects (frequency cannot be estimated from the available data):
- Gas pockets in the bowel.

During treatment it is important to follow the diet that your doctor has recommended carefully. If you do not follow this diet some of the side effects described above such as flatulence (wind), diarrhoea and abdominal pain may be made worse.

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

HOW TO STORE ACARBOSE TABLETS

Keep out of the reach and sight of children. Do not store above 25°C. Store in the original packaging in order to protect from moisture. Do not use Acarbose tablets after the expiry date that is stated on the outer packaging. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

FURTHER INFORMATION

What Acarbose tablets contains:
- The active ingredient is acarbose.
- Each Acarbose 50 mg tablet contains 50 mg acarbose. Each Acarbose 100 mg tablet contains 100 mg acarbose.
- The other ingredients are microcrystalline cellulose, pregelatinized maize starch, anhydrous colloidal silica and magnesium stearate.

What Acarbose tablets looks like and contents of the pack:
- Acarbose 50 mg tablets are round, biconvex, white to off-white tablets with “ACA 50” on one side.
- Acarbose 100 mg tablets are round, biconvex, white to off-white tablets, with a score-line on one side and “ACA 100” on the other side. The scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.
- Acarbose tablets are available in pack sizes of 20, 21, 30, 40, 50, 60, 90, 100, 105, 120 and 270 tablets.

Marketing Authorisation Holder:
TEVA UK Limited
Eastbourne
BN22 9AG
United Kingdom.

Manufacturer:
FAMAR ITALIA S.P.A
Via Zambeletti 25
20021 Baranzate (MI)
Italy.

This leaflet was last revised June 2011

Teva 75522-A
Module 4
Labelling

Carton:

Blister:
Module 5
Scientific discussion during initial procedure

I  INTRODUCTION
Based on the review of the data on quality, safety and efficacy, the member states considered that the applications for Acarbose 50mg and 100mg tablets (PL 00289/1114-5; UK/H/1362/001-2/DC) could be approved.

These applications were submitted by the decentralised procedure, with the UK as Reference Member State (RMS), and Germany, France, Hungary, Poland and Portugal as Concerned Member States (CMS). These products are prescription-only medicines indicated for the treatment of non-insulin dependent diabetes mellitus (NIDDM) in patients inadequately controlled on diet alone, or on diet and (i) metformin and / or (ii) a sulphonylurea.

The Marketing Authorisation Holder has submitted a biowaiver for the need to submit studies of therapeutic equivalence which was accepted by the RMS. These applications are not based on demonstration of bioequivalence and were made via the Decentralised Procedure (DCP), according to Article 10.3 of 2001/83/EC, as amended, a hybrid application. The reference medicinal products for these applications are Glucobay 50 mg and 100 mg tablets, which were originally granted licences on 23 August 1988 to Bayer AG, Belgium.

Acarbose exerts its activity in the intestinal tract (in all species tested). 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.

No new non-clinical studies or clinical were conducted, which is acceptable given that these are hybrid applications with originator products that have been licensed for over 10 years.

The Marketing Authorisation Holder submitted a biowaiver in place of therapeutic equivalence as described below:

The Marketing Authorisation Holder referred to:
• CPMP/EWP/QWP/1401/98 rev 1, 01 August 2010 “Note for guidance on the Investigation of Bioequivalence” and
• CPMP/EWP/239/95 ”Note for guidance on the clinical requirements for locally applied, locally acting products containing known constituents”:

The Marketing Authorisation Holder made the following claims:
• same qualitative and quantitative composition in terms of active substance and the same qualitative composition in terms of excipients of test products (both 50 mg and 100 mg strengths) and corresponding reference formulations (Glucobay 50 and 100 mg, Bayer)
• high solubility and limited absorption of acarbose drug substance (BCS-class III)
• very rapid (>85% within 15 min) dissolution profiles
• the drug substance does not belong to the group of narrow therapeutic index drugs
• site of action of the drug
• a low risk of therapeutic failure

The biowaiver was accepted by the RMS and as a result, new data was not required
The RMS has been assured that acceptable standards of GMP are in place for this product type at all sites responsible for the manufacture, assembly and batch release of this product.

The RMS and CMS considered that the applications could be approved with the end of procedure (Day 210) on 08 June 2011. After a subsequent national phase, the licences were granted in the UK on 28 June 2011.
## II. ABOUT THE PRODUCT

| Name of the product in the Reference Member State | Acarbose 50mg tablets  
Acarbose 100mg tablets |
<table>
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<tr>
<td>Name(s) of the active substance(s) (INN)</td>
<td>Acarbose</td>
</tr>
<tr>
<td>Pharmacotherapeutic classification (ATC code)</td>
<td>Alpha glucosidase inhibitors (A10BF01).</td>
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<tr>
<td>Pharmaceutical form and strength(s)</td>
<td>50mg and 100mg tablets</td>
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<td>Reference Member State</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>Member States concerned</td>
<td>Germany, France, Hungary, Poland and Portugal</td>
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<tr>
<td>Marketing Authorisation Number(s)</td>
<td>PL 00289/1114-5</td>
</tr>
<tr>
<td>Name and address of the authorisation holder</td>
<td>Teva UK Limited, Brampton Road, Hampden Park, Eastbourne, BN22 9AG, UK.</td>
</tr>
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</table>
III SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 QUALITY ASPECTS

S. Active substances

INN: Acarbose

Chemical name: \( O-4,6\text{-Dideoxy-4-[[1(S),4R,5S,6S)-4,5,6-trihydroxy-3-}
\text{(hydroxymethyl)cyclohex-2-enyl]amino}-\alpha-d\text{-glucopyranosyl-}(1\rightarrow4)-}
\text{O-}\alpha-\text{d-glucopyranosyl-(1\rightarrow4)-d-glucopyranose} \)

Structure:

Molecular formula: \( C_{25}H_{43}NO_{18} \)
Molecular weight: 646
Appearance: Acarbose is a white or almost white, amorphous powder. It is extremely soluble in water, soluble in methanol and insoluble in acetone and acetonitrile.

Acarbose is the subject of European Pharmacopoeia monograph

All aspects of the manufacture and control of the active substance acarbose are covered by a European Directorate for the Quality of Medicines (EDQM) Certificate of Suitability.

P. Medicinal Product

Other Ingredients

Other ingredients consist of the pharmaceutical excipients microcrystalline cellulose, pregelatinised maize starch, colloidal anhydrous silica and magnesium stearate.

All excipients comply with their respective European Pharmacopoeia monograph. Suitable batch analysis data have been provided for each excipient, showing compliance with their respective monograph.

None of the excipients contain materials of animal or human origin. No genetically modified organisms (GMO) have been used in the preparation of these products.

Pharmaceutical Development

The objective of the development programme was to formulate stable oral dosage forms that are comparable in performance to the reference products.

A satisfactory account of the pharmaceutical development has been provided.

Comparative in-vitro dissolution and impurity profiles have been provided for the proposed and originator products.

Manufacturing Process

Satisfactory batch formulae have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated on pilot scale batches and has shown satisfactory results.
Finished Product Specifications
The finished product specifications proposed are acceptable. Test methods have been described and have been adequately validated. Batch data have been provided and comply with the release specifications. Certificates of analysis have been provided for all working standards used.

Container-Closure System
The finished product is packaged in polyvinyl chloride/polyethylene/polyvinylidene chloride/aluminium blisters and is available in pack sizes of 20, 21, 30, 40, 50, 60, 90, 100, 105, 120 and 270 tablets.

Satisfactory specifications and certificates of analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

Stability of the product
Stability studies were performed in accordance with current guidelines on batches of the finished product packed in the packaging proposed for marketing. The data from these studies support a shelf-life of 3 years with the storage conditions “Do not store above 25 °C. Store in the original packaging in order to protect from moisture”.

Bioequivalence/bioavailability
Bioequivalence studies are not necessary to support these applications.

The Marketing Authorisation Holder submitted a biowavier in place of therapeutic equivalence as described below:

The Marketing Authorisation Holder referred to:
- CPMP/EWP/QWP/1401/98 rev 1, 01 August 2010 “Note for guidance on the Investigation of Bioequivalence” and
- CPMP/EWP/239/95 "Note for guidance on the clinical requirements for locally applied, locally acting products containing known constituents”:

The Marketing Authorisation Holder made the following claims:
- same qualitative and quantitative composition in terms of active substance and the same qualitative composition in terms of excipients of test products (both 50 mg and 100 mg strengths) and corresponding reference formulations (Glucobay 50 and 100 mg, Bayer)
- high solubility and limited absorption of acarbose drug substance (BCS-class III)
- very rapid (>85% within 15 min) dissolution profiles
- the drug substance does not belong to the group of narrow therapeutic index drugs
- site of action of the drug
- a low risk of therapeutic failure

The biowaver was accepted by the RMS and as a result, new clinical data were not required.
Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL), Labels
The SmPCs, PIL and labels are acceptable.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to understand and act upon the information that it contains.

MAA form
The MAA forms are satisfactory.

Expert report
The pharmaceutical expert report has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical dossier.

Conclusion
There are no objections to the approval of these products from a pharmaceutical viewpoint.

III.2 NON-CLINICAL ASPECTS
As the pharmacodynamic, pharmacokinetic and toxicological properties of acarbose are well-known, no new non-clinical studies are required and none have been provided.

The applicant’s non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the product’s pharmacology and toxicology.

A suitable justification has been provided for non-submission of an environmental risk assessment.
There are no objections to the approval of these products from a non-clinical viewpoint.

III.3 CLINICAL ASPECTS
Pharmacokinetics
No new data have been submitted and none are required.

Pharmacodynamics
Biowavier
The Marketing Authorisation Holder submitted a biowavier in place of therapeutic equivalence as described below:

The Marketing Authorisation Holder referred to:
• CPMP/EWP/QWP/1401/98 rev 1, 01 August 2010 “Note for guidance on the Investigation of Bioequivalence” and
• CPMP/EWP/239/95 "Note for guidance on the clinical requirements for locally applied, locally acting products containing known constituents”:

The Marketing Authorisation Holder made the following claims:
• same qualitative and quantitative composition in terms of active substance and the same qualitative composition in terms of excipients of test products (both 50 mg and 100 mg strengths) and corresponding reference formulations (Glucobay 50 and 100 mg, Bayer)
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• very rapid (>85% within 15 min) dissolution profiles
• the drug substance does not belong to the group of narrow therapeutic index drugs
• site of action of the drug
• a low risk of therapeutic failure

The biowaver was accepted by the RMS and as a result, new data was not required

**Efficacy**

No new data are submitted and none are required for these applications. Efficacy is reviewed in the clinical overview. The efficacy of acarbose is well-established from its extensive clinical use.

**Safety**

No new safety data were submitted and none were required for these applications.

**Pharmacovigilance System and Risk Management Plan**

The Pharmacovigilance System, as described by the applicant, fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance, and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

A suitable justification has been provided for not submitting a Risk Management Plan for these products.

**Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL), Labels**

The SmPCs, PIL and labels are acceptable. The SmPCs are consistent with that for the originator products. The PIL is consistent with the SmPCs and in-line with current guidelines. The labelling is in-line with current guidelines.

**Clinical Expert Report**

The clinical expert report has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

**Conclusion**

There are no objections to the approval of these products from a clinical viewpoint.

**IV OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT**

**QUALITY**

The important quality characteristics of Acarbose 50mg and 100mg tablets are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit-risk balance.

**NON-CLINICAL**

No new non-clinical data were submitted and none are required for applications of this type.

**EFFICACY AND SAFETY**

No new clinical studies were submitted for these applications and none are required.

The MAH requested a biowaver for the these applications based on claims of same qualitative and quantitative composition in terms of active substance and the same *qualitative* composition in terms of excipients of the test generic and reference tablets, high solubility.
and limited absorption of acarbose, rapid and complete dissolution of the dosage form, site of action and low risk of therapeutic failure. The biowaiver criteria specified in CPMP/EWP/QWP/1401/98 Rev 1/Corr and CPMP/EWP/239/95 final have been satisfactorily addressed and support a biowaiver.

No new or unexpected safety concerns arise from this application.

The SmPCs, PIL and labelling are satisfactory

**BENEFIT-RISK ASSESSMENT**

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with acarbose is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is, therefore, considered to be positive.
Module 6

STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY

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<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
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