Core Safety Profile

Active substance: Miglitol
Pharmaceutical form(s)/strength: Tablets 50 mg and 100 mg
P-RMS: NL/H/PSUR/0049/002
Date of FAR: 24.06.2013
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 contraindicated 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 potentiate 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 foetal 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 foetal malformations associated with abnormal blood glucose levels.

**Lactation:**
Miglitol must not be used during lactation (see section 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 antidiabetic treatments (sulfonylureas and insulin), hypoglycaemia has been commonly reported (see section 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.

**Hepato-biliary disorders**
- 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.