2. Loughhead AM, *et al.* Antidepressants in amniotic fluid: another route of fetal exposure. *Am J Psychiatry* 2006; **163:** 145–7.
3. Rampono J, *et al.* A pilot study of newer antidepressant concentrations in cord and maternal serum and possible effects in the neonate. *Int J Neuropsychopharmacol* 2004; **7:** 329–34.

Uses and Administration

Venlafaxine, a phenylethylamine derivative, is a serotonin and noradrenaline reuptake inhibitor (SNRI); it also weakly inhibits dopamine reuptake. It is reported to have little affinity for muscarinic, histaminergic, or α_1-adrenergic receptors *in vitro*. Venlafaxine is given orally as the hydrochloride although doses are expressed in terms of the base; venlafaxine hydrochloride 28.3 mg is equivalent to about 25 mg of venlafaxine.

Venlafaxine is used in the treatment of **depression**. The initial daily dose is equivalent to venlafaxine 75 mg in two or three divided doses with food. In the USA, it is suggested that some patients may be best started on 37.5 mg daily for the first 4 to 7 days before increasing the dose to 75 mg daily. The dose may be increased, if necessary, after several weeks to 150 mg daily. Further increases, to a maximum daily dose of 375 mg, may be made in increments of up to 75 mg at intervals of at least 2 to 4 days. Such doses may be required in severely depressed or hospitalised patients and should be gradually reduced to the minimum effective dose. Modified-release preparations are available for once-daily dosing.

Venlafaxine is also used, as a modified-release preparation, in the treatment of **generalised anxiety disorder**. The recommended initial dose is 75 mg once daily. In the USA it is suggested that some patients may be best begun with 37.5 mg daily for 4 to 7 days initially; dosage may subsequently be adjusted in increments of up to 75 mg, at intervals of at least 4 days, to a maximum of 225 mg daily. Venlafaxine should be withdrawn gradually if there is no response after 8 weeks.

In the USA, modified-release venlafaxine is licensed for the treatment of **social anxiety disorder** in doses similar to those used for generalised anxiety disorder. It is also licensed in the USA for **panic disorder** with or without agoraphobia in doses of 37.5 mg once daily for the first 7 days, then increasing to 75 mg daily. Subsequent increases in increments of up to 75 mg may be made at intervals of at least 7 days, to a maximum dose of 225 mg daily.

Reduced doses may need to be given in hepatic or renal impairment, see below.

Venlafaxine should be withdrawn gradually to reduce the risk of withdrawal symptoms (see Precautions, above).

Administration in hepatic impairment. UK licensed product information considers that patients with mild hepatic impairment do not require a change in dose of venlafaxine. For those with moderate impairment, the dose should be reduced by half and given once daily. There are insufficient data to make any recommendations for patients with severe impairment.

Administration in renal impairment. The UK licensed product information states that, based on glomerular filtration rate (GFR), patients with mild renal impairment (GFR above 30 mL/minute) do not require a change in dose of venlafaxine. For those with moderate impairment (GFR 10 to 30 mL/minute), the dose should be reduced by 50% and once-daily dosage may be appropriate. There are insufficient data to make any recommendations for patients with severe impairment (GFR less than 10 mL/minute).

In the USA, it is recommended that patients with a GFR of 10 to 70 mL/minute reduce the dose of immediate-release venlafaxine by 25% and of modified-release venlafaxine by 25 to 50%; regardless of preparation, in those undergoing haemodialysis, the dose should be reduced by 50% and withheld until the dialysis is completed.

Anxiety disorders. Venlafaxine is used in the treatment of generalised anxiety disorder and social anxiety disorder (see under Phobic Disorders, p.953); it may also be of use in a variety of other types of anxiety disorders (p.952) including the treatment of obsessive-compulsive disorder (p.952), panic disorder (p.952), and post-traumatic stress disorder (p.953).

References.
1. Altamura AC, *et al.* Venlafaxine in social phobia: a study in selective serotonin reuptake inhibitor non-responders. *Int Clin Psychopharmacol* 1999; **14:** 239–45.
2. Gelenberg AJ, *et al.* Efficacy of venlafaxine extended-release capsules in nondepressed outpatients with generalized anxiety disorder: a 6-month randomized controlled trial. *JAMA* 2000; **283:** 3082–8.
3. Sheehan DV. Attaining remission in generalized anxiety disorder: venlafaxine extended release comparative data. *J Clin Psychiatry* 2001; **62** (suppl 19): 26–31.
4. Katz IR, *et al.* Venlafaxine ER as a treatment for generalized anxiety disorder in older adults: pooled analysis of five randomised placebo-controlled clinical trials. *J Am Geriatr Soc* 2002; **50:** 18–25.
5. Hollander E, *et al.* Venlafaxine in treatment-resistant obsessive-compulsive disorder. *J Clin Psychiatry* 2003; **64:** 546–50. Correction. *ibid.*; 972.
6. Lenox-Smith AJ, Reynolds A. A double-blind, randomised, placebo controlled study of venlafaxine XL in patients with generalised anxiety disorder in primary care. *Br J Gen Pract* 2003; **53:** 772–7.
7. Boyer P, *et al.* Social adjustment in generalised anxiety disorder: a long-term placebo-controlled study of venlafaxine extended release. *Eur Psychiatry* 2004; **19:** 272–9.
8. Denys D, *et al.* A double-blind switch study of paroxetine and venlafaxine in obsessive-compulsive disorder. *J Clin Psychiatry* 2004; **65:** 37–43.
9. Liebowitz MR, *et al.* Venlafaxine extended release vs placebo and paroxetine in social anxiety disorder. *Arch Gen Psychiatry* 2005; **62:** 190–8.
10. Liebowitz MR, *et al.* A randomized controlled trial of venlafaxine extended release in generalized social anxiety disorder. *J Clin Psychiatry* 2005; **66:** 238–47.
11. Phelps NJ, Cates ME. The role of venlafaxine in the treatment of obsessive-compulsive disorder. *Ann Pharmacother* 2005; **39:** 136–40.
12. Bradwejn J, *et al.* Venlafaxine extended-release capsules in panic disorder: flexible-dose, double-blind, placebo-controlled study. *Br J Psychiatry* 2005; **187:** 352–9.
13. Davidson J, *et al.* Venlafaxine extended release in posttraumatic stress disorder: a sertraline- and placebo-controlled study. *J Clin Psychopharmacol* 2006; **26:** 259–67. Correction. *ibid.*; 473. [dose]
14. Davidson J, *et al.* Treatment of posttraumatic stress disorder with venlafaxine extended release: a 6-month randomized controlled trial. *Arch Gen Psychiatry* 2006; **63:** 1158–65.
15. Ferguson JM, *et al.* Relapse prevention of panic disorder in adult outpatient responders to treatment with venlafaxine extended release. *J Clin Psychiatry* 2007; **68:** 58–68.

Depression. As discussed on p.373, there is very little difference in efficacy between the different groups of antidepressant drugs, and choice is often made on the basis of adverse effect profile. In December 2004 the UK CSM recommended that, because of the risk of adverse cardiovascular effects and toxicity in overdosage (see above), venlafaxine treatment should be begun and maintained under specialist supervision only. After an assessment of further safety evidence, these restrictions were revised in May 2006 and specialist supervision was considered only necessary when starting venlafaxine treatment in severely depressed or hospitalised patients who require doses of 300 mg daily or above. However, it was also advised that venlafaxine should be considered a second-line treatment, after the SSRIs.

The *O*-desmethyl metabolite of venlafaxine, desvenlafaxine (p.388), is also used in depression.

References.
1. Morton WA, *et al.* Venlafaxine: a structurally unique and novel antidepressant. *Ann Pharmacother* 1995; **29:** 387–95.
2. Derivan A, *et al.* Venlafaxine: measuring the onset of antidepressant action. *Psychopharmacol Bull* 1995; **31:** 439–47.
3. Wellington K, Perry CM. Venlafaxine extended-release: a review of its use in the management of major depression. *CNS Drugs* 2001; **15:** 643–69.
4. Cohen LS, *et al.* Venlafaxine in the treatment of postpartum depression. *J Clin Psychiatry* 2001; **62:** 592–6.
5. Montgomery SA, *et al.* Venlafaxine versus placebo in the preventive treatment of recurrent major depression. *J Clin Psychiatry* 2004; **65:** 328–36.

Hot flushes. For the reference to the use of venlafaxine in the treatment of hot flushes, see under Fluoxetine, p.398.

Hyperactivity. When drug therapy is indicated for attention deficit hyperactivity disorder (p.2148) initial treatment is usually with a central stimulant. Antidepressants may be used for patients who fail to respond to, or who are intolerant of, central stimulants; in open studies venlafaxine has been reported to be effective in both adults[1-3] and children[4,5] although in one study[4] some patients experienced a worsening of symptoms.

1. Hedges D, *et al.* An open trial of venlafaxine in adult patients with attention deficit hyperactivity disorder. *Psychopharmacol Bull* 1995; **31:** 779–83.
2. Adler LA, *et al.* Open-label trial of venlafaxine in adults with attention deficit disorder. *Psychopharmacol Bull* 1995; **31:** 785–8.
3. Findling RL, *et al.* Venlafaxine in adults with attention-deficit/hyperactivity disorder: an open clinical trial. *J Clin Psychiatry* 1996; **57:** 184–9.
4. Olvera RL, *et al.* An open trial of venlafaxine in the treatment of attention-deficit/hyperactivity disorder in children and adolescents. *J Child Adolesc Psychopharmacol* 1996; **6:** 241–50.
5. Motavalli Mukaddes N, Abali O. Venlafaxine in children and adolescents with attention deficit hyperactivity disorder. *Psychiatry Clin Neurosci* 2004; **58:** 92–5.

Migraine. Retrospective analysis[1] in patients with tension-type headache (p.617) or migraine (p.616) indicated that venlafaxine, as a modified-release preparation, had potential for headache prophylaxis. A more recent randomised placebo-controlled study[2] also supports the use of modified-release venlafaxine in the prophylaxis of migraine.

1. Adelman LC, *et al.* Venlafaxine extended release (XR) for the prophylaxis of migraine and tension-type headache: a retrospective study in a clinical setting. *Headache* 2000; **40:** 572–80.
2. Ozyalcin SN, *et al.* The efficacy and safety of venlafaxine in the prophylaxis of migraine. *Headache* 2005; **45:** 144–52.

Pain. Venlafaxine may be of benefit in the treatment of neuropathic pain syndromes (p.8)[1,2] including painful diabetic neuropathy (p.6).[3-5] It has also shown some promise in the treatment of fibromyalgia (see Soft-tissue Rheumatism, p.13).[6]

1. Sumpton JE, Moulin DE. Treatment of neuropathic pain with venlafaxine. *Ann Pharmacother* 2001; **35:** 557–9.
2. Grothe DR, *et al.* Treatment of pain syndromes with venlafaxine. *Pharmacotherapy* 2004; **24:** 621–9.
3. Davis JL, Smith RL. Painful peripheral diabetic neuropathy treated with venlafaxine HCl extended release capsules. *Diabetes Care* 1999; **22:** 1909–10.
4. Kiayias JA, *et al.* Venlafaxine HCl in the treatment of painful peripheral diabetic neuropathy. *Diabetes Care* 2000; **23:** 699.
5. Rowbotham MC, *et al.* Venlafaxine extended release in the treatment of painful diabetic neuropathy: a double-blind, placebo-controlled study. *Pain* 2004; **110:** 697–706. Correction. *ibid.* 2005; **113:** 248.
6. Sayar K, *et al.* Venlafaxine treatment of fibromyalgia. *Ann Pharmacother* 2003; **37:** 1561–5.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Efexor; Elafax; Ganavax; Mezine; Quilarex; Sesaren; ***Austral.:*** Efexor; ***Austria:*** Efectin; ***Belg.:*** Efexor; ***Braz.:*** Efexor; Venlaxin; Venlift; ***Canad.:*** Effexor; ***Chile:*** Depurol; Efexor; Nervix; Norpilen; Senexon; Sentidol; Sesaren; Subelan; Venlax; ***Cz.:*** Argofan; Convalemin; Efectin; Elify; Faxiprol; Lafaxon; Mollome; Olvexya; Velaxin; ***Denm.:*** Efexor; ***Fin.:*** Efexor; ***Fr.:*** Effexor; ***Ger.:*** Trevilor; ***Gr.:*** Arvifax; Efexor; ***Hong Kong:*** Efexor; ***Hung.:*** Efectin; Olwexya; Velaxin; ***India:*** Flavix; Venlor; Vexor; ***Indon.:*** Efexor; ***Irl.:*** Efexor; ***Israel:*** Efexor; Venla; Viepax; ***Ital.:*** Efexor; Faxine; ***Malaysia:*** Efexor; ***Mex.:*** Efexor; Odven SBK; ***Neth.:*** Efexor; ***Norw.:*** Efexor; ***NZ:*** Efexor; ***Philipp.:*** Efexor; ***Pol.:*** Efectin; Velafax; Velaxin; ***Port.:*** Desinax; Efexor; Genexin; Venxin; Xapnev; Zarelix; ***Rus.:*** Efevelone (Эфевелон); Velafax (Велафакс); Velaxin (Велаксин); ***S.Afr.:*** Efexor; Venlor; ***Singapore:*** Efexor; ***Spain:*** Dobupal; Vandral; ***Swed.:*** Efexor; ***Switz.:*** Efexor; ***Thai.:*** Efexor; ***Turk.:*** Efexor; ***UK:*** Efexor; ***USA:*** Effexor; ***Venez.:*** Efexor; Idoxen; Sesaren.

Viloxazine Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de viloxazina; ICI-58834; Viloxazine, Chlorhydrate de; Viloxazini Hydrochloridum. 2-(2-Ethoxyphenoxymethyl) morpholine hydrochloride.

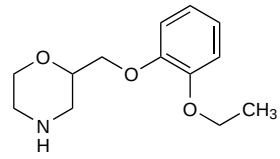
Вилоксазина Гидрохлорид

$C_{13}H_{19}NO_3$,HCl = 273.8.

CAS — 46817-91-8 (viloxazine); 35604-67-2 (viloxazine hydrochloride).

ATC — N06AX09.

ATC Vet — QN06AX09.



(viloxazine)

Profile

Viloxazine is a bicyclic antidepressant. Like the tricyclic antidepressants (see Amitriptyline, p.376), viloxazine is an inhibitor of the reuptake of noradrenaline; it may also enhance the release of serotonin from neuronal stores. However, it does not have marked antimuscarinic, cardiotoxic, or sedative properties.

Viloxazine is given for the treatment of depression (p.373) as the hydrochloride although doses are expressed in terms of viloxazine; viloxazine hydrochloride 57.7 mg is equivalent to about 50 mg of viloxazine. The usual oral dose is equivalent to viloxazine 200 to 300 mg daily in 2 or 3 divided doses. This may be increased, if necessary, to 600 mg daily as tolerated. The initial dose for the elderly or patients with hepatic or renal impairment is 100 mg daily cautiously increased if necessary. A modified-release preparation is also available for once daily use. Viloxazine hydrochloride has also been given by intravenous infusion.

Viloxazine should be withdrawn gradually to reduce the risk of withdrawal symptoms.

Porphyria. Viloxazine hydrochloride is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Vivalan†; ***Cz.:*** Vivalan†; ***Fr.:*** Vivalan†; ***Ger.:*** Vivalan†; ***Port.:*** Vivalan†.

For further details on the treatment of insulin-induced hypoglycaemia, see p.447.

Diabetic ketoacidosis is caused by an absolute or relative lack of insulin and commonly occurs after noncompliance or failure to adjust insulin dosage in the presence of factors such as infection that increase insulin requirements (see Precautions for Insulin, p.447). Failure of an insulin pump can be a cause.[5] Also pregnant diabetic women are more prone to development of diabetic ketoacidosis.

Diabetic ketoacidosis is characterised by hyperglycaemia, hyperketonaemia, and acidaemia, with subsequent dehydration and electrolyte abnormalities. Onset may be rapid, or insidious over many days. Initial presenting symptoms such as thirst, polyuria, fatigue, and weight loss are those of any newly presenting type 1 diabetic; they then progress to nausea, vomiting, abdominal pain, and impaired consciousness or coma, and, if untreated, death.[5,6]

Diabetic ketoacidosis is a medical emergency and should be treated immediately with fluid replacement and insulin.[5-8] Fluid requirements depend on the needs of the individual; overvigorous fluid replacement without severe dehydration carries the risk of precipitating cerebral oedema.[6-8]

Soluble insulin should also be given immediately. Large doses were formerly thought necessary, but lower dose regimens accompanied by adequate hydration have since been shown to be preferable.[5] Insulin resistance in diabetic ketoacidosis is generally exacerbated by hyperosmolarity and other confounding factors, and insulin therapy is therefore most effective when preceded or accompanied by adequate fluid and electrolyte replacement.[5] In the UK, the *BNF* considers that insulin should preferably be given by intravenous infusion, with the intramuscular route used if facilities for intravenous infusion are not available. However, in the USA some consider that an intravenous bolus followed by subcutaneous injection may be appropriate in certain patients.[5] Intramuscular or subcutaneous injection are not appropriate in patients with hypovolaemic shock, due to poor tissue perfusion.[5] Where the response to insulin is inadequate the intravenous route is generally required[5] and the rate of infusion may be doubled on an hourly basis until an appropriate response is seen. A case report has suggested that mecasermin may be useful if there is insulin resistance.[9]

When the blood-glucose concentration has fallen to about 12.5 mmol/litre the dose of insulin may be reduced by about half and glucose given intravenously,[5] usually in a strength of 5% with saline although in rare cases a glucose strength of 10% may be necessary.[5] The use of glucose enables insulin to be continued in order to clear ketone bodies without inducing hypoglycaemia. Once glucose concentrations have been controlled and acidosis has completely cleared, subcutaneous injections of insulin can begin;[6] but intravenous insulin should not be stopped until subcutaneous dosage has begun.

Total body stores of potassium are depleted in patients with diabetic ketoacidosis. Insulin deficiency appears to be the main initiating factor for hyperkalaemia in diabetic ketoacidosis.[10] Although patients may present with raised, normal, or decreased serum-potassium concentrations, the concentrations will start to fall with the correction of acidosis. Potassium is added to the infusion fluid after initial fluid expansion and once insulin therapy has begun.[5] In hyperkalaemic patients, potassium is given once serum concentrations have fallen to within normal limits.[5,6] In the rare patient presenting with hypokalaemia potassium replacement should be begun before insulin therapy and the latter withheld until potassium concentrations have risen to normal values.[5]

Intravenous bicarbonate is now generally reserved for patients with severe acidaemia; a common practice[5,6] is to give isotonic bicarbonate to those with a pH of less than 7.0 with the aim of raising the pH to 7.1.

Phosphate concentrations are affected in a similar manner to potassium concentrations in the ketoacidotic state, but there is less agreement on the need for routine doses of phosphate. Phosphate concentrations should be monitored and phosphate given if clinically significant hypophosphataemia occurs.[5,6]

The precipitating cause of diabetic ketoacidosis should also be identified and managed appropriately.

Hyperosmolar hyperglycaemic state or hyperosmolar hyperglycaemic nonketotic coma (HONK) occurs mainly in elderly patients with type 2 diabetes and though much less common than diabetic ketoacidosis it carries a higher mortality. Patients may present in coma with severe hyperglycaemia but with minimal ketosis; dehydration and renal impairment are common.[5] Treatment is similar to that of diabetic ketoacidosis (see above), although potassium requirements are lower and large amounts of fluid and less insulin may be required; some suggest the use of hypotonic fluid if necessary.[11] There is an increased likelihood of thrombotic events, so prophylactic anticoagulation should be considered.

1. Cranston I, *et al.* Restoration of hypoglycaemia awareness in patients with long-duration insulin-dependent diabetes. *Lancet* 1994; **344:** 283–7.
2. Boyle PJ, *et al.* Brain glucose uptake and unawareness of hypoglycemia in patients with insulin-dependent diabetes mellitus. *N Engl J Med* 1995; **333:** 1726–31.
3. Debrah K, *et al.* Effect of caffeine on recognition of and physiological responses to hypoglycaemia in insulin-dependent diabetes. *Lancet* 1996; **347:** 19–24.
4. Watson JM, *et al.* Influence of caffeine on the frequency and perception of hypoglycemia in free-living patients with type 1 diabetes. *Diabetes Care* 2000; **23:** 455–9.
5. Kitabchi AE, *et al.* Management of hyperglycemic crises in patients with diabetes. *Diabetes Care* 2001; **24:** 131–53.
6. Lebovitz HE. Diabetic ketoacidosis. *Lancet* 1995; **345:** 767–72.
7. Adrogué HJ, *et al.* Salutary effects of modest fluid replacement in the treatment of adults with diabetic ketoacidosis: use in patients without extreme volume deficit. *JAMA* 1989; **262:** 2108–13.
8. Johnston C. Fluid replacement in diabetic ketoacidosis. *BMJ* 1992; **305:** 522.
9. Usala A-L, *et al.* Brief report: treatment of insulin-resistant diabetic ketoacidosis with insulin-like growth factor I in an adolescent with insulin-dependent diabetes. *N Engl J Med* 1992; **327:** 853–7.
10. Anonymous. Hyperkalaemia in diabetic ketoacidosis. *Lancet* 1986; **ii:** 845–6.
11. Wright AD. Diabetic emergencies in adults. *Prescribers' J* 1989; **29:** 147–54.

Acarbose *(BAN, USAN, rINN)*

Acarbosa; Acarbosum; Akarboosi; Akarbos; Akarbosa; Akarboz; Akarbozė; Bay-g-5421. *O*-{4-Amino-4,6-dideoxy-*N*-[(1*S*,4*R*,5*S*,6*S*)-4,5,6-trihydroxy-3-hydroxymethylcyclohex-2-enyl]-α-D-glucopyranosyl}-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-D-glucopyranose.

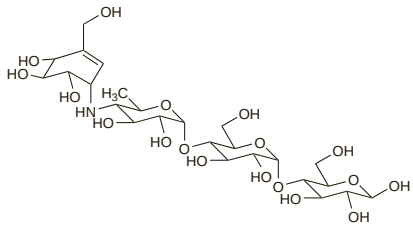
Акарбоза

$C_{25}H_{43}NO_{18}$ = 645.6.

CAS — 56180-94-0.

ATC — A10BF01.

ATC Vet — QA10BF01.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*

Ph. Eur. 6.2 (Acarbose). A white or yellowish, amorphous, hygroscopic powder. Very soluble in water; practically insoluble in dichloromethane; soluble in methyl alcohol. A 5% solution in water has a pH of 5.5 to 7.5. Store in airtight containers.

USP 31 (Acarbose). Produced by certain strains of *Actinoplanes utahensis*. Store in airtight containers.

Adverse Effects

Acarbose often causes gastrointestinal disturbances, particularly flatulence due to bacterial action on nonabsorbed carbohydrate in the colon. Abdominal distension, diarrhoea, and pain may occur. Ileus has been rarely reported. A decrease in dosage and improved dietary habits may reduce these adverse effects. Hepatotoxicity may occur and may necessitate a reduction in dosage or withdrawal of the drug. Skin reactions have occurred rarely. Very rarely oedema has been reported.

Incidence of adverse effects. The manufacturers reported that adverse effects of acarbose were rarer in a postmarketing surveillance study than in previous clinical trials;[1] this was held to represent better tailoring of individual doses to patient tolerability.

1. Spengler M, Cagatay M. The use of acarbose in the primary-care setting: evaluation of efficacy and tolerability of acarbose by postmarketing surveillance study. *Clin Invest Med* 1995; **18:** 325–31.

Effects on the liver. Hepatocellular liver damage, with jaundice and elevated serum aminotransferases, have been reported in patients receiving acarbose.[1-3] Symptoms resolved on stopping the drug.

1. Andrade RJ, *et al.* Hepatic injury caused by acarbose. *Ann Intern Med* 1996; **124:** 931.
2. Carrascosa M, *et al.* Acarbose-induced acute severe hepatotoxicity. *Lancet* 1997; **349:** 698–9.
3. Fujimoto Y, *et al.* Acarbose-induced hepatic injury. *Lancet* 1998; **351:** 340.

Effects on the skin. Generalised erythema multiforme and eosinophilia occurred in a male diabetic patient 13 days after starting acarbose.[1] The hypersensitivity reaction was confirmed by rechallenge.

1. Kono T, *et al.* Acarbose-induced generalised erythema multiforme. *Lancet* 1999; **354:** 396–7.

Precautions

Acarbose is contra-indicated in inflammatory bowel disease, particularly where there is associated ulceration, and in gastrointestinal obstruction or patients predisposed to it. It should be avoided in patients with chronic intestinal diseases that significantly affect digestion or absorption, and in conditions which may deteriorate as a result of increased gas formation, such as hernia.

Acarbose is also contra-indicated in patients with hepatic impairment and liver enzyme values should be monitored, particularly at high doses.

If hypoglycaemia should develop in a patient receiving acarbose it needs to be treated with glucose, since the action of acarbose inhibits the hydrolysis of disaccharides.

Breast feeding. In the absence of evidence, licensed product information recommends that acarbose should be avoided during breast feeding.

Interactions

Acarbose may enhance the effects of other antidiabetics, including insulin, and a reduction in their dosage may be needed. Use with gastrointestinal adsorbents and digestive enzyme preparations can diminish the effects of acarbose and should be avoided. Neomycin and colestyramine may enhance the effects of acarbose and a reduction in its dosage may be required. Acarbose may inhibit the absorption of digoxin (see Antidiabetics, under Interactions of Digoxin, p.1261).

Pharmacokinetics

After ingestion of acarbose, the majority of active unchanged drug remains in the lumen of the gastrointestinal tract to exert its pharmacological activity and is metabolised by intestinal enzymes and by the microbial flora. Ultimately about 35% of a dose is absorbed in the form of metabolites. Acarbose is excreted in the urine and faeces.

Uses and Administration

Acarbose is an inhibitor of alpha glucosidases, especially sucrase. This slows the digestion and absorption of carbohydrates in the small intestine and hence reduces the increase in blood-glucose concentrations after a carbohydrate load. It is given in the treatment of type 2 diabetes mellitus (p.431) either alone or with a sulfonylurea, biguanide, or insulin. Acarbose treatment may be started with a low oral dose of 25 or 50 mg daily to minimise gastrointestinal disturbance. It is then gradually increased to a usual dose of 25 or 50 mg three times daily, immediately before food. Doses up to 100 to 200 mg three times daily may be given if necessary. Some benefit has also been found when acarbose is used to supplement insulin therapy in type 1 diabetes mellitus.

Acarbose has also been studied for the treatment of reactive hypoglycaemia, the dumping syndrome, and certain types of hyperlipoproteinaemia.

◊ References.

1. Chiasson J-L, *et al.* The efficacy of acarbose in the treatment of patients with non-insulin-dependent diabetes mellitus: a multicenter controlled clinical trial. *Ann Intern Med* 1994; **121:** 928–35.