2. Coniff RF, *et al.* Multicenter, placebo-controlled trial comparing acarbose (BAY g 5421) with placebo, tolbutamide, and tolbutamide-plus-acarbose in non-insulin-dependent diabetes mellitus. *Am J Med* 1995; **98:** 443–51.
3. 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.
4. Salvatore T, Giugliano D. Pharmacokinetic-pharmacodynamic relationships of acarbose. *Clin Pharmacokinet* 1996; **30:** 94–106.
5. Anonymous. Acarbose for diabetes mellitus. *Med Lett Drugs Ther* 1996; **38:** 9–10.
6. Hoffman J, Spengler M. Efficacy of 24-week monotherapy with acarbose, metformin, or placebo in dietary-treated NIDDM patients: the Essen-II study. *Am J Med* 1997; **103:** 483–90.
7. Hollander P, *et al.* Acarbose in the treatment of type I diabetes. *Diabetes Care* 1997; **20:** 248–53.
8. Buse J, *et al.* The PROTECT study: final results of a large multicenter postmarketing study in patients with type 2 diabetes. *Clin Ther* 1998; **20:** 257–69.
9. Holman RR, *et al.* A randomized double-blind trial of acarbose in type 2 diabetes shows improved glycemic control over 3 years (UK Prospective Diabetes Study 44). *Diabetes Care* 1999; **22:** 960–4.
10. Riccardi G, *et al.* Efficacy and safety of acarbose in the treatment of type 1 diabetes mellitus: a placebo-controlled, double-blind, multicentre study. *Diabet Med* 1999; **16:** 228–32.
11. Chiasson J-L, *et al.* Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. *Lancet* 2002; **359:** 2072–7.

Impaired glucose tolerance. A prospective study of patients with impaired glucose tolerance concluded that acarbose significantly reduced the incidence of cardiovascular disease and hypertension.[1]

1. Chiasson J-L, *et al.* Acarbose treatment and the risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance: the STOP-NIDDM trial. *JAMA* 2003; **290:** 486–94.

Preparations

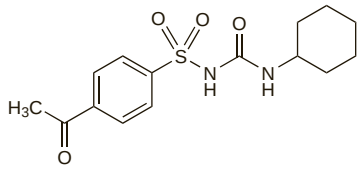
Proprietary Preparations (details are given in Part 3)
Arg.: Glucobay; ***Austral.:*** Glucobay; ***Austria:*** Glucobay; ***Belg.:*** Glucobay; ***Braz.:*** Aglucose; Glucobay; ***Canad.:*** Prandase; ***Chile:*** Glucobay; ***Cz.:*** Glucobay; ***Denm.:*** Glucobay; ***Fr.:*** Glucor; ***Ger.:*** Glucobay; ***Gr.:*** Glucobay; ***Hong Kong:*** Glucobay; ***Hung.:*** Glucobay; ***India:*** Acarbay; Asucrose; Glubose; Glucar; Glucobay; ***Indon.:*** Glucobay; ***Irl.:*** Glucobay; ***Israel:*** Prandase; ***Ital.:*** Glicobase; Glucobay; ***Malaysia:*** Dibose; Glucar; Glucobay; Precose; ***Mex.:*** Glucobay; Incardel; Sincrosa; ***Neth.:*** Glucobay; ***Norw.:*** Glucobay; ***NZ:*** Glucobay; ***Philipp.:*** Glucobay; Gluconase; ***Pol.:*** Glucobay; ***Port.:*** Glucobay; ***Rus.:*** Glucobay (Глюкобай); ***S.Afr.:*** Glucobay; ***Singapore:*** Glucobay; ***Spain:*** Glucobay; Glumida; ***Swed.:*** Glucobay; ***Switz.:*** Glucobay; ***Thai.:*** Glucobay; ***Turk.:*** Glucobay; Glynose; ***UK:*** Glucobay; ***USA:*** Precose; ***Venez.:*** Glucobay.

Acetohexamide *(BAN, USAN, rINN)*

Acetohexamid; Acetohexamida; Acétohexamide; Acetohexamidum; Asetoheksamidi; Compound 33006. 1-(4-Acetylbenzenesulphonyl)-3-cyclohexylurea.

Ацетогексамид

$C_{15}H_{20}N_2O_4S$ = 324.4.
CAS — 968-81-0.
ATC — A10BB31.
ATC Vet — QA10BB31.



Pharmacopoeias. In *Jpn* and *US*.
USP 31 (Acetohexamide). A white, practically odourless, crystalline powder. Practically insoluble in water and in ether; soluble 1 in 230 of alcohol and 1 in 210 of chloroform; soluble in pyridine and in dilute solutions of alkali hydroxides.

Profile
Acetohexamide is a sulfonylurea antidiabetic (p.460). Its duration of action is 12 hours or more. It has been given orally in the treatment of type 2 diabetes mellitus (p.431) in a usual initial dose of 250 mg daily before breakfast. The daily dose may then be increased by 250 to 500 mg at intervals of 5 to 7 days, to a maintenance dose of up to 1.5 g daily; increasing the dose above 1.5 g does not usually lead to further benefit. Doses in excess of 1 g daily may be taken in 2 divided doses, before the morning and evening meals.

Preparations
USP 31: Acetohexamide Tablets.

Proprietary Preparations (details are given in Part 3)
USA: Dymelor†.

Biguanide Antidiabetics

Antidiabéticos biguanídicos.

Adverse Effects
Gastrointestinal adverse effects including anorexia, nausea, vomiting, and diarrhoea may occur with biguanides; patients may experience taste disturbance and there may be weight loss. Absorption of various substances including vitamin B_{12} may be impaired. Skin reactions have been reported rarely.

Hypoglycaemia is rare with a biguanide given alone, although it may occur if other contributing factors or drugs are present.

Lactic acidosis, sometimes fatal, has occurred with biguanides, primarily with phenformin. When it has occurred with metformin most cases have been in patients whose condition contra-indicated the use of the drug, particularly those with renal impairment.

Phenformin has been implicated in the controversial reports of excessive cardiovascular mortality associated with oral hypoglycaemic therapy (see under Sulfonylureas, Effects on the Cardiovascular System, p.461).

◊ Reviews.

1. Paterson KR, *et al.* Undesired effects of biguanide therapy. *Adverse Drug React Acute Poisoning Rev* 1984; **3:** 173–82.
2. Howlett HCS, Bailey CJ. A risk-benefit assessment of metformin in type 2 diabetes mellitus. *Drug Safety* 1999; **20:** 489–503.

Effects on the blood. Megaloblastic anaemia has occurred with biguanide therapy (see Malabsorption, under Effects on the Gastrointestinal Tract, below). A few cases of metformin-induced haemolysis resulting in hyperbilirubinaemia and jaundice have also been described.[1,2]

1. Lin K-D, *et al.* Metformin-induced hemolysis with jaundice. *N Engl J Med* 1998; **339:** 1860–1.
2. Meir A, *et al.* Metformin-induced hemolytic anemia in a patient with glucose-6-phosphate dehydrogenase deficiency. *Diabetes Care* 2003; **26:** 956–7.

Effects on the gastrointestinal tract. ***DIARRHOEA.*** In a retrospective survey,[1] 30 of 265 diabetic patients reported diarrhoea or alternating diarrhoea and constipation, comprising: 11 of 54 taking metformin; 9 of 45 taking metformin with a sulfonylurea; 3 of 53 taking a sulfonylurea only; 5 of 78 on insulin therapy; 2 of 35 on diet alone. Among 150 nondiabetic controls 12 reported diarrhoea. Chronic diarrhoea described as watery, often explosive, and frequently causing faecal incontinence, has been reported as an adverse effect of late onset in patients receiving metformin. Some patients had been on stable metformin therapy for several years before the onset of diarrhoea. Symptoms ceased upon withdrawal of metformin, and recurred in cases of rechallenge.[2,3]

1. Dandona P, *et al.* Diarrhea and metformin in a diabetic clinic. *Diabetes Care* 1983; **6:** 472–4.
2. Raju B, *et al.* Metformin and late gastrointestinal complications. *Am J Med* 2000; **109:** 260–1.
3. Foss MT, Clement KD. Metformin as a cause of late-onset chronic diarrhea. *Pharmacotherapy* 2001; **21:** 1422–4.

MALABSORPTION. Megaloblastic anaemia due to vitamin B_{12} malabsorption in a 58-year-old woman was associated with long-term treatment with metformin.[1]

In a survey of diabetic patients receiving biguanide therapy,[2] malabsorption of vitamin B_{12} was observed in 14 of 46 diabetics taking metformin or phenformin; metformin was more commonly to blame. Withdrawal of the drug resulted in normal absorption in only 7 of the 14. In a series of 10 patients[3] with vitamin B_{12} deficiency associated with metformin, vitamin B_{12} concentrations and blood count abnormalities were reported to have been corrected within 3 months of starting treatment with intramuscular or oral cyanocobalamin; 2 patients were transferred to treatment with other antidiabetic agents.

1. Callaghan TS, *et al.* Megaloblastic anaemia due to vitamin B malabsorption associated with long-term metformin treatment. *BMJ* 1980; **280:** 1214–15.
2. Adams JF, *et al.* Malabsorption of vitamin B and intrinsic factor secretion during biguanide therapy. *Diabetologia* 1983; **24:** 16–18.
3. Andrès E, *et al.* Metformin-associated vitamin B deficiency. *Arch Intern Med* 2002; **162:** 2251–2.

Effects on the liver. Severe cholestatic hepatitis attributed to metformin has been reported.[1]

1. Babich MM, *et al.* Metformin-induced acute hepatitis. *Am J Med* 1998; **104:** 490–2.

Effects on the pancreas. Acute pancreatitis is more commonly associated with phenformin.[1,2] However, there have also been a few cases of pancreatitis associated with metformin, in which renal failure may have precipitated metformin toxicity.[3,4]

1. Wilde H. Pancreatitis and phenformin. *Ann Intern Med* 1972; **77:** 324.
2. Chase HS, Mogan GR. Phenformin-associated pancreatitis. *Ann Intern Med* 1977; **87:** 314–15.
3. Mallick S. Metformin induced acute pancreatitis precipitated by renal failure. *Postgrad Med J* 2004; **80:** 239–40.
4. Fimognari FL, *et al.* Metformin-induced pancreatitis: a possible adverse drug effect during acute renal failure. *Diabetes Care* 2006; **29:** 1183.

Hypersensitivity. Vasculitis and pneumonitis in a 59-year-old woman was associated with use of metformin.[1] Symptoms improved on withdrawal of metformin, but reappeared on its reintroduction. Cutaneous vasculitis in a 33-year-old woman also resolved on withdrawal of metformin and recurred with its reintroduction.[2]

1. Klapholz L, *et al.* Leucocytoclastic vasculitis and pneumonitis induced by metformin. *BMJ* 1986; **293:** 483.
2. Salem CB, *et al.* Rare case of metformin-induced leukocytoclastic vasculitis. *Ann Pharmacother* 2006; **40:** 1685–7.

Hypoglycaemia. UK licensed product information for metformin states that hypoglycaemia does not occur with metformin alone, even in overdosage, although it may occur if given with alcohol or other hypoglycaemics. Interim results from the UK Prospective Diabetes Study,[1] however, indicate that metformin therapy was associated with fewer hypoglycaemic episodes than sulfonylurea or insulin treatment, but more than with diet alone. One or more hypoglycaemic episodes were reported in 6% of the patients receiving the biguanide in this study, although only 1 patient had a severe episode.

1. United Kingdom Prospective Diabetes Study Group. United Kingdom prospective diabetes study (UKPDS) 13: relative efficacy of randomly allocated diet, sulphonylurea, insulin, or metformin in patients with newly diagnosed non-insulin dependent diabetes followed for 3 years. *BMJ* 1995; **310:** 83–8.

Lactic acidosis. There is a small but definite risk of lactic acidosis associated with use of biguanide antidiabetics. Most early reports involved phenformin, which was consequently removed from the market in many countries although cases of phenformin-associated lactic acidosis still occur.[1-3] There has therefore been concern about the risks of lactic acidosis with metformin, which is still in wide use. However, lactic acidosis with metformin appears to be much less common: a review suggested that the incidence was of the order of 3 cases per 100 000 patient years, which was 20 times less frequent than with phenformin.[4] This concurs with the findings of the FDA after the introduction of metformin to the US market: in the year after the marketing of metformin in the USA, the FDA had received reports of metformin-associated lactic acidosis in 66 patients,[5] the diagnosis being confirmed in 47. This represented a rate of about 5 cases per 100 000. Most patients who do develop lactic acidosis with metformin have one or more precipitating risk factors such as renal impairment, congestive heart failure, or other conditions predisposing to hypoxaemia or acute renal failure, including septicaemia, acute hepatic decompensation, alcohol abuse, acute myocardial infarction, and shock.[4] A systematic review,[6] which considered results comprising nearly 48 000 patient years of treatment with metformin, concluded that provided metformin was prescribed taking into account the proper contra-indications, there was no evidence of an increased risk of lactic acidosis. Nonetheless, there have been a few reports of lactic acidosis developing in metformin-treated patients without apparent risk factors.[4]

1. Rosand J, *et al.* Fatal phenformin-associated lactic acidosis. *Ann Intern Med* 1997; **127:** 170.
2. Enia G, *et al.* Lactic acidosis induced by phenformin is still a public health problem in Italy. *BMJ* 1997; **315:** 1466–7.
3. Kwong SC, Brubacher J. Phenformin and lactic acidosis: a case report and review. *J Emerg Med* 1998; **16:** 881–6.
4. Chan NN, *et al.* Metformin-associated lactic acidosis: a rare or very rare clinical entity? *Diabet Med* 1999; **16:** 273–81.
5. Misbin RI, *et al.* Lactic acidosis in patients with diabetes treated with metformin. *N Engl J Med* 1998; **338:** 265–6.
6. Salpeter S, *et al.* Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2006 (accessed 02/05/06).

Treatment of Adverse Effects
Acute poisoning with biguanides may lead to the development of lactic acidosis (see Metabolic Acidosis, p.1667) and calls for intensive supportive therapy. Glucose or glucagon may be required for hypoglycaemia, the general management of which is outlined in Insulin, p.447.

Precautions
Biguanides are inappropriate for patients with diabetic coma and ketoacidosis, or for those with severe infection, trauma, or other severe conditions where the biguanide is unlikely to control the hyperglycaemia; insulin should be used in such situations. Biguanides should not be given to patients with even mild renal impairment, as it may predispose patients to lactic acidosis, and renal function should be monitored throughout therapy. Dehydration may contribute to renal impairment. Conditions associated with hypoxia, such as

acute heart failure, recent myocardial infarction, or shock, may increase the risk of lactic acidosis. Other conditions that may also predispose to lactic acidosis in a patient taking a biguanide include excessive alcohol intake and hepatic impairment. Biguanides should be temporarily stopped for examinations using contrast media (see under Interactions, below).

Insulin is preferred for the treatment of diabetes in pregnancy.

Owing to the possibility of decreased vitamin B_{12} absorption, annual monitoring of vitamin B_{12} concentrations is advisable during long-term treatment.

Driving. In the UK, patients with diabetes mellitus treated with insulin or oral hypoglycaemics are required to notify their condition to the Driver and Vehicle Licensing Agency, who then assess their fitness to drive. Patients treated with oral hypoglycaemics are generally allowed to retain standard driving licences; those treated with insulin receive restricted licences which must be renewed (with appropriate checks) every 1 to 3 years. Patients should be warned of the dangers of hypoglycaemic attacks while driving, and should be counselled in appropriate management of the situation (stopping driving as soon as it is safe to do so, taking carbohydrate immediately, and quitting the driving seat and removing the ignition key from the car) should such an event occur. Patients who have lost hypoglycaemic awareness, or have frequent hypoglycaemic episodes, should not drive. In addition, eyesight must be adequate (field of vision of at least 120°) for a licence to be valid. Patients treated with diet or oral hypoglycaemics are normally allowed to hold vocational driving licences for heavy goods vehicles or passenger carrying vehicles; those treated with insulin may not drive such vehicles, and are restricted in driving some other vehicles such as small lorries and minibuses.

References.

1. British Diabetic Association (Diabetes UK). Information sheet: driving and diabetes: May 2008. Available at: http://www.diabetes.org.uk/Documents/catalogue/driving_and_diabetes-may_08.pdf (accessed 20/08/08)
2. Driver and Vehicle Licensing Agency. For medical practitioners: at a glance guide to the current medical standards of fitness to drive (February 2008). Available at: http://www.dvla.gov.uk/media/pdf/medical/aagv1.pdf (accessed 14/08/08)

Interactions

Use of a biguanide with other drugs that lower blood-glucose concentrations increases the risk of hypoglycaemia, while drugs that increase blood glucose may reduce the effect of biguanide therapy.

In general fewer drug interactions have been reported with biguanides than with sulfonylureas. Alcohol may increase the risk of lactic acidosis as well as of hypoglycaemia. Care should be taken if biguanides are given with drugs that may impair renal function.

Anticoagulants. For the effect of metformin on *phenprocoumon* activity, see Antidiabetics, p.1428.

Antivirals. Fatal lactic acidosis has been reported[1] in a patient given metformin with *didanosine*, *stavudine*, and *tenofovir*.

1. Worth L, *et al*. A cautionary tale: fatal lactic acidosis complicating nucleoside analogue and metformin therapy. *Clin Infect Dis* 2003; **37:** 315–16.

Cimetidine. Cimetidine increased plasma-metformin concentrations in 7 healthy subjects.[1] The renal clearance of metformin was reduced; competition for proximal tubular secretion was considered responsible. A reduction in metformin dosage may be required in patients taking metformin and cimetidine, in order to reduce the risk of lactic acidosis.

1. Somogyi A, *et al*. Reduction of metformin renal tubular secretion by cimetidine in man. *Br J Clin Pharmacol* 1987; **23:** 545–51.

Contrast media. Biguanides should be temporarily stopped for examinations using iodinated contrast media and withheld after the examination until normal renal function is confirmed, because of the risk of contrast media-induced renal impairment leading to biguanide toxicity and associated lactic acidosis. Licensed product information for some contrast media preparations warns that biguanides should be temporarily stopped 48 hours before the examination, and withheld for at least 48 hours after and until normal renal function is confirmed.

A number of guidelines on the use of iodinated contrast media give advice for the management of patients taking metformin. Some suggest that, in general, metformin can be stopped at the time of the examination.[1,2] Others are more detailed, suggesting that if serum-creatinine is normal metformin may be stopped at the time of the examination, but that if it is raised metformin should be stopped 48 hours before giving the contrast medium.[3,4] They all agree that metformin should be withheld for 48 hours after the examination and until normal renal function is confirmed, although one suggests that no special precaution is needed for patients with normal serum-creatinine who are to be given a low volume of iodinated contrast medium (up to 100 mL).[3]

1. Committee on Drugs and Contrast Media, Commission on General and Pediatric Radiology of the American College of Radiology. Manual on contrast media, 5th ed. Available at: http://www.acr.org/SecondaryMainMenuCategories/quality_safety/contrast_manual.aspx (accessed 26/06/07)
2. Benko A, *et al*. Canadian Association of Radiologists: consensus guidelines for the prevention of contrast-induced nephropathy. *Can Assoc Radiol J* 2007; **58:** 79–87. Correction available at: http://www.car.ca/Files%5CNephropathy.pdf (accessed 20/08/08) [correct version]
3. Board of the Faculty of Clinical Radiology; The Royal College of Radiologists. Standards for iodinated intravascular contrast agent administration to adult patients (issued November 2005). Available at: http://www.rcr.ac.uk/docs/radiology/pdf/IVcontrastPrintFinal.pdf (accessed 26/06/07)
4. European Society of Urogenital Radiology. ESUR guidelines on contrast media (version 6.0, issued February 2007). Available at: http://www.esur.org/fileadmin/Guidelines/ESUR_2007_Guideline_6_Kern_Ubersicht.pdf (accessed 26/06/07)

Ketotifen. Platelet counts in 10 diabetic patients receiving biguanides fell (markedly in 3 patients) when they were also given ketotifen.[1] Counts returned to normal a few days after the end of ketotifen therapy. However, the investigators did not consider the effect clinically significant.

1. Doleček R. Ketotifen in the treatment of diabetics with various allergic conditions. *Pharmatherapeutica* 1981; **2:** 568–74.

Sulfonylureas. For reference to an apparent increase in mortality with an intensive regimen of metformin plus a sulfonylurea, see p.462.

Uses and Administration

The biguanide antidiabetics are a class of oral antidiabetic drugs used in the treatment of type 2 diabetes mellitus (p.431). They are given to supplement treatment by diet modification when such modification has not proved effective on its own. In addition, because biguanides are not associated with weight gain they are preferred in obese patients. Although sulfonylureas (p.460) may be preferred in non-obese patients, a biguanide is often added or given instead to patients who are not responding to a sulfonylurea.

The mode of action of biguanides is not clear. They do not stimulate insulin release but require that some insulin be present in order to exert their antidiabetic effect. Possible mechanisms of action include delay in the absorption of glucose from the gastrointestinal tract, an increase in insulin sensitivity and glucose uptake into cells, and inhibition of hepatic gluconeogenesis. Biguanides do not usually lower blood-glucose concentrations in non-diabetic subjects.

Hyperlipidaemias. The effect of biguanides on lipid metabolism is unclear, although some studies have shown a beneficial effect on serum-lipid profiles in both obese and lean patients with type 2 diabetes, hypertension, and/or hyperlipidaemia.[1] Reductions in concentrations of total cholesterol, low-density and very low-density-lipoprotein cholesterol have been reported, as well as modest increases in high-density-lipoprotein cholesterol. Some studies have also reported a reduction in serum-triglyceride levels. Such effects may be beneficial in the long-term treatment of type 2 diabetes mellitus with concomitant lipid disorders.

1. Dunn CJ, Peters DH. Metformin: a review of its pharmacological properties and therapeutic use in non-insulin-dependent diabetes mellitus. *Drugs* 1995; **49:** 721–49.

Polycystic ovary syndrome. For discussion of the potential of metformin in polycystic ovary syndrome, see p.454.

Preparations

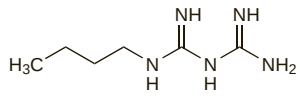
Proprietary Preparations (details are given in Part 3)
Mex.: Azucaps†.
Multi-ingredient: ***Mex.:*** Glinorboral.

Buformin *(USAN, pINN)*

Buformina; Buformine; Buforminum; DBV; W-37. 1-Butylbiguanide.

Буформин

$C_6H_{15}N_5$ = 157.2.
CAS — 692-13-7 (buformin); 1190-53-0 (buformin hydrochloride).
ATC — A10BA03.
ATC Vet — QA10BA03.



Profile

Buformin is a biguanide antidiabetic (p.437). It has been given orally in the treatment of type 2 diabetes mellitus (p.431) in doses of up to 300 mg daily. Buformin is also used as the hydrochloride.

Preparations

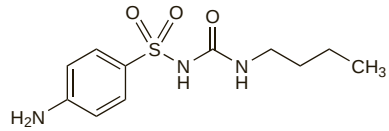
Proprietary Preparations (details are given in Part 3)
Cz.: Adebit†; Silubin†; ***Hung.:*** Adebit; ***Spain:*** Silubin†; ***Switz.:*** Silubin†.

Carbutamide *(BAN, rINN)*

BZ-55; Ca-1022; Carbutamida; Carbutamidum; Glybutamide; Karbutamid; Karbutamidi; U-6987. 1-Butyl-3-sulphanilylurea.

Карбутамид

$C_{11}H_{17}N_3O_3S$ = 271.3.
CAS — 339-43-5.
ATC — A10BB06.
ATC Vet — QA10BB06.



Profile

Carbutamide is a sulfonylurea antidiabetic (p.460). It is given orally in the treatment of type 2 diabetes mellitus (p.431) in single daily doses of 0.5 to 1 g, but is more toxic than chlorpropamide.

Preparations

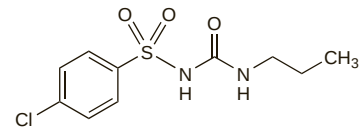
Proprietary Preparations (details are given in Part 3)
Fr.: Glucidoral.

Chlorpropamide *(BAN, rINN)*

Chloropropamid; Chlorpropamid; Chlorpropamidas; Chlorrpropamidum; Clorpropamida; Klooripropamidi; Klórpropamid; Klorpropamid. 1-(4-Chlorobenzenesulphonyl)-3-propylurea.

Хлорпропамид

$C_{10}H_{13}ClN_2O_3S$ = 276.7.
CAS — 94-20-2.
ATC — A10BB02.
ATC Vet — QA10BB02.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Chlorpropamide). A white or almost white, crystalline powder. It exhibits polymorphism. Practically insoluble in water; soluble in alcohol; freely soluble in acetone and in dichloromethane; dissolves in dilute solutions of alkali hydroxides. Protect from light.
USP 31 (Chlorpropamide). A white crystalline powder having a slight odour. Practically insoluble in water; soluble in alcohol; sparingly soluble in chloroform.

Adverse Effects and Treatment

As for sulfonylureas in general, p.460.

Chlorpropamide may be more likely than other sulfonylureas to induce a syndrome of inappropriate secretion of antidiuretic hormone characterised by water retention, hyponatraemia, and CNS effects. Patients receiving chlorpropamide may develop facial flushing after drinking alcohol.

Precautions

As for sulfonylureas in general, p.461.

Chlorpropamide should be avoided in the elderly and in renal or hepatic impairment because its long half-life increases the risk of hypoglycaemia. The antidiuretic effect of chlorpropamide may cause problems in patients with conditions associated with fluid retention.

Fasting. For the view that although some sulfonylurea antidiabetics may be able to be used with caution in fasting Muslim patients during Ramadan, chlorpropamide is contra-indicated, see under Precautions of Insulin, p.448.