Porphyria. Chlorpropamide has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Thyroid disorders. Some manufacturers recommend that chlorpropamide should not be used in patients with impaired thyroid function, but see under Sulfonylureas, p.461.

Interactions

As for sulfonylureas in general, p.461.

Chlorpropamide may produce profound facial flushing associated with alcohol ingestion.

Pharmacokinetics

Chlorpropamide is readily absorbed from the gastrointestinal tract and is extensively bound to plasma proteins. The half-life is about 35 hours. About 80% of a dose is metabolised in the liver; metabolites and unchanged drug are excreted in the urine. Chlorpropamide crosses the placenta and has been detected in breast milk.

Uses and Administration

Chlorpropamide is a sulfonylurea antidiabetic (p.460). It has a duration of action of at least 24 hours, and is given orally in the treatment of type 2 **diabetes mellitus** (p.431) in an initial daily dose of 250 mg as a single dose with breakfast. After 5 to 7 days the dose may be adjusted, in steps of 50 to 125 mg at intervals of 3 to 5 days, to achieve an optimum maintenance dose which is usually in the range 100 to 500 mg daily. Increasing the dose above 500 mg daily is unlikely to produce further benefit, and doses above 750 mg daily should be avoided. Although a reduced dose range has been proposed for the elderly, use of chlorpropamide is inadvisable in this group.

Chlorpropamide, though not the other sulfonylureas, is also sometimes used in cranial **diabetes insipidus** (p.2179). It has been reported to act by sensitising the renal tubules to antidiuretic hormone. The dose has to be carefully adjusted to minimise the risk of hypoglycaemia. An initial dose of 100 mg daily, adjusted if necessary to a maximum of 350 mg daily has been recommended, although doses of up to 500 mg daily have been used.

Diabetes mellitus. Patients with type 2 diabetes whose blood glucose is adequately controlled at first by sulfonylureas often eventually have treatment failure and loss of diabetic control. Results from the UK Prospective Diabetes Study[1] have suggested that the 6-year failure rate was higher in patients treated with glibenclamide (48%) than in those given chlorpropamide (40%). This difference was equivalent to delaying the requirement for additional therapy for a year in chlorpropamide-treated patients.

1. Matthews DR, *et al.* UKPDS 26: sulphonylurea failure in non-insulin-dependent diabetic patients over six years. *Diabet Med* 1998; **15:** 297–303.

Preparations

BP 2008: Chlorpropamide Tablets;
USP 31: Chlorpropamide Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Diabinese; Idle†; Trane; ***Belg.:*** Diabinese†; ***Braz.:*** Clorpromini†; Clorzin†; Diabecontrol; Diabinese; Glicoben; Glicorp; Pramidalin; ***Canad.:*** Novo-Propamide; ***Chile:*** Diabinese; ***Gr.:*** Diabinese; ***Hong Kong:*** Diabinese; ***India:*** Copamide†; ***Indon.:*** Diabinese; ***Israel:*** Diabinese†; Diabitex; ***Ital.:*** Diabemide; ***Malaysia:*** Anti-D†; Diabinese†; Propamide; ***Mex.:*** Aposprod; Diabiclor; Diabinese; Insogen; ***Philipp.:*** Diabinese; ***S.Afr.:*** Diabinese; Hypomide; ***Singapore:*** Anti-D; Chlomide†; Diabinese†; Propamide; ***Spain:*** Diabinese; ***Thai.:*** Diabeedol; Diabinese; Dibecon; Glycemin; Propamide; ***Turk.:*** Diabinese; ***USA:*** Diabinese; ***Venez.:*** Dabinese.

Multi-ingredient: ***India:*** Chlorformin†; ***Ital.:*** Bidiabe; Pleiamide; ***Mex.:*** Insogen Plus; Mellitron; Obinese; ***Switz.:*** Diabiformine.

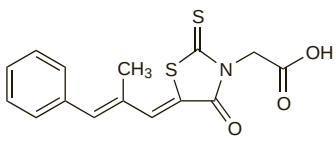
Epalrestat *(rINN)*

Épalrestat; Epalrestatum; ONO-2235. 5-[(*Z*,*E*)-β-Methylcinnamylidene]-4-oxo-2-thioxo-3-thiazolidineacetic acid.

Эпалрестат

$C_{15}H_{13}NO_3S_2$ = 319.4.

CAS — 82159-09-9.



Profile

Epalrestat inhibits the enzyme aldose reductase which catalyses the conversion of glucose to sorbitol. It has been suggested that accumulation of sorbitol in certain cells, occurring only in conditions of hyperglycaemia and resulting in a hyperosmotic effect, may be involved in the pathogenesis of some diabetic complications. Aldose reductase inhibitors have no influence on blood-glucose concentrations. Epalrestat is given orally for the treatment of diabetic complications including neuropathy (p.433), in a usual dose of 50 mg three times daily before meals.

◊ References.

1. Goto Y, *et al.* A placebo-controlled double-blind study of epalrestat (ONO-2235) in patients with diabetic neuropathy. *Diabet Med* 1993; **10** (suppl 2): 39S–43S.
2. Uchida K, *et al.* Effect of 24 weeks of treatment with epalrestat, an aldose reductase inhibitor, on peripheral neuropathy in patients with non-insulin-dependent diabetes mellitus. *Clin Ther* 1995; **17:** 460–6.
3. Hotta N, *et al.* Clinical investigation of epalrestat, an aldose reductase inhibitor, on diabetic neuropathy in Japan: multicenter study. *J Diabetes Complications* 1996; **10:** 168–72.
4. Ikeda T, *et al.* Long-term effect of epalrestat on cardiac autonomic neuropathy in subjects with non-insulin dependent diabetes mellitus. *Diabetes Res Clin Pract* 1999; **43:** 193–8.
5. Iso K, *et al.* Long-term effect of epalrestat, an aldose reductase inhibitor, on the development of incipient diabetic nephropathy in type 2 diabetic patients. *J Diabetes Complications* 2001; **15:** 241–4.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Kinedak.

Exenatide *(BAN, USAN, rINN)*

AC-2993; AC-002993; AC-2993A; Exenatida; Exénatide; Exenatidum; LY-2148568; Synthetic Exendin-4.

Эксенатид

$C_{184}H_{282}N_{50}O_{60}S$ = 4186.6.

CAS — 141758-74-9 (exenatide); 141732-76-5 (exendin-4).

ATC — A10BX04.

ATC Vet — QA10BX04.

H–His–Gly–Glu–Gly–Thr–Phe–Thr–Ser–Asp–Leu–
10
Ser–Lys–Gln–Met–Glu–Glu–Glu–Ala–Val–Arg–
20
Leu–Phe–Ile–Glu–Trp–Leu–Lys–Asn–Gly–Gly–
30
Pro–Ser–Ser–Gly–Ala–Pro–Pro–Pro–Ser–NH_2
39

Adverse Effects and Precautions

Hypoglycaemia can occur in patients given exenatide, particularly when given with a sulfonylurea (see also Interactions, below). Exenatide commonly causes mild to moderate nausea, which is dose-dependent and tends to decrease with continued therapy in most patients. Other adverse effects include vomiting, diarrhoea, nervousness, dizziness, headache, and dyspepsia. Less frequent reports include asthenia, decreased appetite, gastro-oesophageal reflux, and hyperhidrosis. Rashes and hypersensitivity reactions have occurred rarely. Acute pancreatitis has been reported, and in such cases exenatide should be stopped permanently.

Exenatide should not be used in type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Use is not recommended in patients with severe renal impairment, in whom clearance is reduced and adverse gastrointestinal effects have been reported.

Effects on the pancreas. A 69-year-old man developed pancreatitis within a few days of starting exenatide therapy. Serum-lipase concentrations returned to normal and abdominal pain resolved rapidly when exenatide was stopped.[1] The FDA has also reviewed 30 reports of acute pancreatitis in patients treated with exenatide.[2] In 27 cases there was at least one other risk factor for acute pancreatitis such as gallstones, severe hypertriglyceridaemia, and alcohol use. Improvement after stopping exenatide was confirmed in 22 reports, and in 3 cases of rechallenge there was a return of symptoms of acute pancreatitis. The FDA subsequently reported[3] in August 2008 that they had received reports of 6 cases of haemorrhagic or necrotising pancreatitis associated with exenatide; all patients required hospitalisation and 2 died. It was recommended that exenatide therapy should be stopped if signs or symptoms of pancreatitis develop and should not be restarted if pancreatitis is confirmed. Other antidiabetic drugs should be considered for those with a history of pancreatitis.

1. Denker PS, Dimarco PE. Exenatide (exendin-4)-induced pancreatitis: a case report. *Diabetes Care* 2006; **29:** 471.
2. FDA. Information for healthcare professionals: exenatide (marketed as Byetta) (issued October 2007). Available at: http://www.fda.gov/cder/drug/InfoSheets/HCP/exenatideHCP.htm (accessed 17/10/07)
3. FDA. Information for healthcare professionals: exenatide (marketed as Byetta) (issued August 2008). Available at: http://www.fda.gov/cder/drug/InfoSheets/HCP/exenatide2008HCP.htm (accessed 20/08/08)

Interactions

A reduction in the sulfonylurea dose may be required when exenatide is added to therapy, because of an increased risk of hypoglycaemia with this combination. No increase in hypoglycaemia occurs when exenatide is used with metformin or a thiazolidinedione. The extent and rate of absorption of oral drugs may be reduced by exenatide. Where such an interaction would be undesirable, the oral medication should be given at least 1 hour before exenatide. If the oral medication is to be taken with food, where possible, it should be with a meal or snack when exenatide is not used.

Pharmacokinetics

After subcutaneous injection, peak plasma concentrations of exenatide are reached in about 2 hours. It is eliminated through the kidneys by glomerular filtration followed by proteolytic degradation, with a terminal half-life of about 2.4 hours. Clearance is reduced in patients receiving dialysis for end-stage renal disease.

◊ References.

1. Kolterman OG, *et al.* Pharmacokinetics, pharmacodynamics, and safety of exenatide in patients with type 2 diabetes mellitus. *Am J Health-Syst Pharm* 2005; **62:** 173–81.
2. Linnebjerg H, *et al.* Effect of renal impairment on the pharmacokinetics of exenatide. *Br J Clin Pharmacol* 2007; **64:** 317–27.

Uses and Administration

Exenatide is a synthetic form of exendin-4, a 39-amino acid peptide isolated from the venom of the Gila monster lizard (*Heloderma suspectum*, Helodermatidae). The drug is an incretin mimic that acts as an agonist at the glucagon-like peptide 1 receptor to enhance insulin secretion in the presence of raised glucose concentrations; it also suppresses inappropriate glucagon secretion and slows gastric emptying. Exenatide is used as adjunctive therapy in type 2 diabetes mellitus (p.431) in patients who do not have adequate glycaemic control with metformin, a sulfonylurea, a thiazolidinedione, or dual therapy with metformin plus a sulfonylurea or thiazolidinedione. It is given by subcutaneous injection in an initial dose of 5 micrograms twice daily within 60 minutes before the morning and evening meals. The dose of exenatide may be increased after 1 month to 10 micrograms twice daily if required.

◊ References.

1. Fineman MS, *et al.* Effectiveness of progressive dose-escalation of exenatide (exendin-4) in reducing dose-limiting side effects in subjects with type 2 diabetes. *Diabetes Metab Res Rev* 2004; **20:** 411–17.
2. Buse JB, *et al.* Effects of exenatide (exendin-4) on glycemic control over 30 weeks in sulfonylurea-treated patients with type 2 diabetes. *Diabetes Care* 2004; **27:** 2628–35.
3. Kendall DM, *et al.* Effects of exenatide (exendin-4) on glycemic control over 30 weeks in patients with type 2 diabetes treated with metformin and a sulfonylurea. *Diabetes Care* 2005; **28:** 1083–91.
4. DeFronzo RA, *et al.* Effects of exenatide (exendin-4) on glycemic control and weight over 30 weeks in metformin-treated patients with type 2 diabetes. *Diabetes Care* 2005; **28:** 1092–1100.
5. Heine RJ, *et al.* Exenatide versus insulin glargine in patients with suboptimally controlled type 2 diabetes: a randomized trial. *Ann Intern Med* 2005; **143:** 559–69.
6. Yoo BK, *et al.* Exenatide: a new option for the treatment of type 2 diabetes. *Ann Pharmacother* 2006; **40:** 1777–84.
7. Ratner RE, *et al.* Long-term effects of exenatide therapy over 82 weeks on glycaemic control and weight in over-weight metformin-treated patients with type 2 diabetes mellitus. *Diabetes Obes Metab* 2006; **8:** 419–28.
8. Nauck MA, *et al.* A comparison of twice-daily exenatide and biphasic insulin aspart in patients with type 2 diabetes who were suboptimally controlled with sulfonylurea and metformin: a non-inferiority study. *Diabetologia* 2007; **50:** 259–67.
9. Zinman B, *et al.* The effect of adding exenatide to a thiazolidinedione in suboptimally controlled type 2 diabetes: a randomized trial. *Ann Intern Med* 2007; **146:** 477–85. Correction. *ibid.*; 896.
10. Cvetković RS, Plosker GL. Exenatide: a review of its use in patients with type 2 diabetes mellitus (as an adjunct to metformin and/or a sulfonylurea). *Drugs* 2007; **67:** 935–54.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Byetta; ***Austral.:*** Byetta; ***Braz.:*** Byetta; ***Cz.:*** Byetta; ***Port.:*** Byetta; ***UK:*** Byetta; ***USA:*** Byetta.

Glibenclamide *(BAN, rINN)*

Glibenclamida; Glibenclamidum; Glibenklamid; Glibenklamidas; Glibenklamidi; Glybenclamide; Glybenzcyclamide; Glyburide *(USAN)*; HB-419; U-26452. 1-{4-[2-(5-Chloro-2-methoxybenzamido)ethyl]benzenesulphonyl}-3-cyclohexylurea.

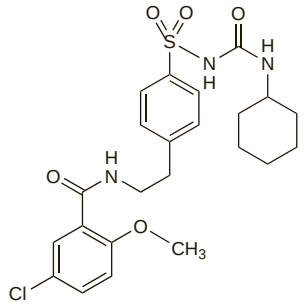
Глибенкламид

$C_{23}H_{28}ClN_3O_5S$ = 494.0.

CAS — 10238-21-8.

ATC — A10BB01.

ATC Vet — QA10BB01.



NOTE. The name glibornuride has frequently but erroneously been applied to glibenclamide.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*.

Ph. Eur. 6.2 (Glibenclamide). A white or almost white, crystalline powder. Practically insoluble in water; slightly soluble in alcohol and in methyl alcohol; sparingly soluble in dichloromethane.

USP 31 (Glyburide). Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for sulfonylureas in general, p.460.

◊ For a suggestion that the failure rate in type 2 diabetics treated with glibenclamide may be higher than that for those treated with chlorpropamide, see Diabetes Mellitus under Uses and Administration of Chlorpropamide, p.439.

Effects on the blood. References.

1. Nataas OB, Nesthus I. Immune haemolytic anaemia induced by glibenclamide in selective IgA deficiency. *BMJ* 1987; **295:** 366–7.
2. Israeli A, *et al*. Glibenclamide causing thrombocytopenia and bleeding tendency: case reports and a review of the literature. *Klin Wochenschr* 1988; **66:** 223–4.
3. Meloni G, Meloni T. Glyburide-induced acute haemolysis in a G6PD-deficient patient with NIDDM. *Br J Haematol* 1996; **92:** 159–60.
4. Noto H, *et al*. Glyburide-induced hemolysis in myelodysplastic syndrome. *Diabetes Care* 2000; **23:** 129.

Hypoglycaemia. Severe hypoglycaemia may occur in any patient given any sulfonylurea (see p.461); glibenclamide which has a relatively prolonged duration of action, may cause severe hypoglycaemia more often than shorter-acting sulfonylureas.

In a 1983 review[1] of 57 instances of hypoglycaemia associated with glibenclamide the median age of patients affected was 70 years; only one was less than 60 years old. Median daily dosage was 10 mg. Coma or disturbed consciousness was seen in 46 patients. Ten of these remained comatose despite alleviation of their hypoglycaemia and died up to 20 days after presentation. The authors noted that, including their series of 57 cases, there had been published reports on 101 cases of severe hypoglycaemia with glibenclamide, 14 with a fatal outcome.

There has been a report[2] of hypoglycaemic coma associated with the inhalation of glibenclamide by a worker at a pharmaceutical plant.

1. Asplund K, *et al*. Glibenclamide-associated hypoglycaemia: a report on 57 cases. *Diabetologia* 1983; **24:** 412–17.
2. Albert F, *et al*. Hypoglycaemia by inhalation. *Lancet* 1993; **342:** 47–8.

Porphyria. Glibenclamide has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions

As for sulfonylureas in general, p.461.

Pharmacokinetics

Glibenclamide is readily absorbed from the gastrointestinal tract, peak plasma concentrations usually occurring within 2 to 4 hours, and is extensively bound to plasma proteins. Absorption may be slower in hyperglycaemic patients and may differ according to the particle size of the preparation used. It is metabolised, almost completely, in the liver, the principal metabolite being only very weakly active. About 50% of a dose is excreted in the urine and 50% via the bile into the faeces.

◊ References.

1. Coppack SW, *et al*. Pharmacokinetic and pharmacodynamic studies of glibenclamide in non-insulin dependent diabetes mellitus. *Br J Clin Pharmacol* 1990; **29:** 673–84.
2. Jaber LA, *et al*. The pharmacokinetics and pharmacodynamics of 12 weeks of glyburide therapy in obese diabetics. *Eur J Clin Pharmacol* 1993; **45:** 459–63.
3. Hoffman A, *et al*. The effect of hyperglycaemia on the absorption of glibenclamide in patients with non-insulin-dependent diabetes mellitus. *Eur J Clin Pharmacol* 1994; **47:** 53–5.
4. Rydberg T, *et al*. Concentration-effect relations of glibenclamide and its active metabolites in man: modelling of pharmacokinetics and pharmacodynamics. *Br J Clin Pharmacol* 1997; **43:** 373–81.

Uses and Administration

Glibenclamide is a sulfonylurea antidiabetic (p.460). It is given orally in the treatment of type 2 diabetes mellitus (p.431) and has a duration of action of up to 24 hours.

The usual initial dose of conventional formulations in type 2 diabetes mellitus is 2.5 to 5 mg daily with breakfast, adjusted every 7 days in steps of 2.5 or 5 mg daily up to 15 mg daily. Although increasing the dose above 15 mg is unlikely to produce further benefit, doses of up to 20 mg daily have been given. Doses greater than 10 mg daily may be given in 2 divided doses. Because of the relatively long duration of action of glibenclamide, it is best avoided in the elderly.

In some countries micronised preparations of glibenclamide are available, in which the drug is formulated with a smaller particle size, and which have enhanced bioavailability. The usual initial dose of one such preparation (*Glynase PresTab; Pharmacia Upjohn, USA*) is 1.5 to 3 mg daily, adjusted every 7 days in steps of 1.5 mg, up to a usual maximum of 12 mg daily. Doses greater than 6 mg daily may be given in 2 divided doses.

Action. Proceedings of a symposium on the mechanism of action of glibenclamide.[1]

1. Gavin JR, ed. Glyburide: new insights into its effects on the beta cell and beyond. *Am J Med* 1990; **89** (suppl 2A): 1–53S.

EFFECTS ON THE HEART. A reduced incidence of ventricular fibrillation has been reported in diabetics treated with glibenclamide who develop myocardial infarction, compared with those receiving other treatments or with nondiabetic patients with myocardial infarction.[1] However, some evidence has also suggested that sulfonylureas may impair the adaptive responses of the heart to ischaemia—see p.461.

1. Lomuscio A, *et al*. Effects of glibenclamide on ventricular fibrillation in non-insulin-dependent diabetes with acute myocardial infarction. *Coron Artery Dis* 1994; **5:** 767–71.

Preparations

BP 2008: Glibenclamide Tablets;
USP 31: Glyburide and Metformin Hydrochloride Tablets; Glyburide Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Agobilina; Benclamid; Daonil; Diabe Pass; Diabemin; Euglucon; Gardoton; Glentor; Glibediab†; Glibemida; Glidanil; Gliptid; Glitral; GON; Pira; Siruc; ***Austral.:*** Daonil; Glimel; Semi-Daonil; ***Austria:*** Daonil; Dia-Eptal; Euglucon; Gilemal; Glucobene; Glucostad; Normoglucon; Semi-Euglucon; ***Belg.:*** Bevoren; Daonil; Euglucon; ***Braz.:*** Aglucil; Benclamin; Clamiben; Daonil; Diaben; Diabetty's†; Diabexil; Euglucon; Gliben†; Glibenclamon; Glibendiab; Glibexil†; Glicamin; Glionil; Lisaglucon; Uni Glibent†; ***Canad.:*** DiaBeta; Euglucon; Gen-Glybe; ***Chile:*** Daonil; Euglusid; Mezalit; ***Cz.:*** Betanase†; Glibenhexal†; Glucobene; Humedia†; Maninil; ***Denm.:*** Daonil; Hexaglucon; Regulin†; ***Fin.:*** Daonil†; Euglamin; Euglucon; Origlucon; Semi-Euglucon; ***Fr.:*** Daonil; Euglucan; Hemi-Daonil; Miglucan; ***Ger.:*** Azuglucon†; Bastiverit†; duraglucon N; Euglucon N; Glib; Glib-ratiopharm; Gliben; Gliben-Azu†; Gliben-Puren N†; Glibenbeta; Glibendoc; Glibenhexal; Glimidstada†; Glucoremed†; Glukoreduct†; Glukovital; glycolande N†; Humedia; Jutaglucon†; Maninil; Praeciglucon†; Semi-Euglucon N; ***Gr.:*** Daonil; Derocty; Diabefar†; ***Hong Kong:*** Calabren†; Clamide; Daonil; Euglucon; Gliben; Gliboral; Glimel; Glitisol; Marglucon; Semi-Daonil†; Semi-Euglucon; Xeltic; ***Hung.:*** Gilemal; Glucobene; Maninil; ***India:*** Daonil; Euglucon; Glinil; Glybovin; Semi-Daonil; Semi-Euglucon; ***Indon.:*** Condiabet; Daonil; Glidanil; Glimel; Gluconic; Glulo; Glyamid; Libroni; Prodiabet; Prodiamel; Renabetic; Semi-Daonil; Tiabet; Trodeb; ***Irl.:*** Daonil; Semi-Daonil; ***Israel:*** Daonil†; Glibetic; Gluben; ***Ital.:*** Daonil; Euglucon; Gliben; Gliboral; ***Jpn:*** Euglucon; ***Malaysia:*** Claben†; Daonil; Debtan†; Dibelet; Gliben; Glibesyn; Glimide; ***Mex.:*** Abuglib; Apogly; Biostin; Daonil; Dibetid; Diglexol; Euglucon; Gadinor; Glemicid; Glibenil; Glibenval; Glicavin; Glicoxem; Glifarcal; Glihexal; Glikeyer†; Glipar; Glucal; Glucoven; Insusym; Mibeclag; Nadib†; Norboral; Ocrix; Reglusan; ***Neth.:*** Daonil; Hemi-Daonil†; ***Norw.:*** Daonil†; ***NZ:*** Gliben; ***Philipp.:*** Amecladin; Daonil; Diabitor; Euglucon; Eundin; Gluban; Glymod; Insol; Lodulce; Orabetic; Semi-Euglucon; Sentionyl; Sucron; ***Pol.:*** Euclamin; ***Port.:*** Daonil; Euglucon; Semi-Daonil; Semi-Euglucon†; ***Rus.:*** Betanase (Бетаназ); Glibamide (Глибамид)†; Glibex (Глибекс); Glidanil (Глиданил); Maninil (Маниниl); ***S.Afr.:*** Daonil; Diacare; Euglucon†; Glycomin; ***Singapore:*** Clamide; Daonil; Dibelet; GBN†; Glibemid†; Glibesyn; Glimel; Glimide; ***Spain:*** Daonil; Euglucon; Glucolon; Norglicem; ***Swed.:*** Daonil; Euglucon; ***Switz.:*** Daonil; Euglucon; gli-basan; Glibenorme; Glibesifar; Melix; Semi-Daonil; Semi-Euglucon†; ***Thai.:*** Benclamin; BNIL; Cytagon†; Daonil; Daono; Debtan; Diabenol; Dibelet; Diclanil; Euglucon; Glencamide†; Gliben†; Glibetic; Glibic; Gluconil; Gluzo; Locose; Manoglucon; Med-Glionil†; Semi-Euglucon†; Sugril; Unil; Xeltic; ***Turk.:*** Dianorm; Diyaben; Gliben; ***UAE:*** Glynase; Mini-Glynase; ***UK:*** Daonil; Diabetamide†; Euglucon†; Semi-Daonil†; ***USA:*** DiaBeta; Glynase; Micronase; ***Venez.:*** Daonil; Euglucon; Gliciron.

Multi-ingredient: ***Arg.:*** DBI Duo; Glucovance; Isloglib; Medobis G; Metformin Duo; ***Austral.:*** Glucovance; ***Belg.:*** Glucovance; ***Braz.:*** Glucovance; ***Chile:*** Bi-Euglucon M; Diaglitab Plus; Glifortex-G; Glimet; Glucovance; Glukaut; Hipoglucin DA; ***Cz.:*** Glibomet; Glucovance; ***Fr.:*** Glucovance; ***Gr.:*** Daopar†; Normell; ***Hong Kong:*** Glucovance; ***India:*** Diaforte; Glinil M; ***Indon.:*** Glucovance; ***Ital.:*** Bi-Euglucon M; Bi-Euglucon†; Gliben F; Glibomet; Gliconorm; Glicorest; Gliformin; Glucomide; Suguan M; Suguan†; ***Malaysia:*** Glucovance; ***Mex.:*** Apometglu; Bi-Dizalon; Bi-Euglucon M; Bi-Pradia; Duo-Anglucid; Glinorboral; Glucotec; Glucovance; Imalet; Insusym-Forte; Maviglin; Midapharma; Mifelar-C; Nadib-M; Norfaben M; Sibet-C; Sil-Norboral; Wadil; ***Neth.:*** Glucovance; ***Philipp.:*** Euglo Plus; Glucovance; ***Port.:*** Glucovance; ***Rus.:*** Glibomet (Глибомет); Glucovance (Глюкован); ***S.Afr.:*** Glucovance; ***Singapore:*** Glucovance; ***Switz.:*** Glucovance; ***USA:*** Diofen; Glucovance; Glybofen; ***Venez.:*** Bi-Euglucon; Diaformina Plus; Glucovance.

Glibornuride *(BAN, USAN, rINN)*

Glibornurid; Glibornurida; Glibornuridi; Glibornuridum; Ro-6-4563. 1-[(2*S*,3*R*)-2-Hydroxyborn-3-yl]-3-tosylurea; 1-[(2*S*,3*R*)-2-Hydroxyborn-3-yl]-3-*p*-tolylsulphonylurea.

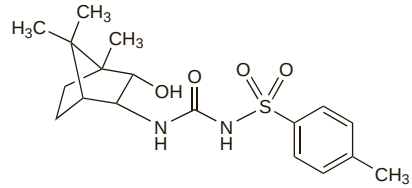
Глиборнурид

$C_{18}H_{26}N_2O_4S$ = 366.5.

CAS — 26944-48-9.

ATC — A10BB04.

ATC Vet — QA10BB04.



NOTE. The name glibornuride has frequently but erroneously been applied to glibenclamide.

Profile

Glibornuride is a sulfonylurea antidiabetic (p.460). It is given orally in the treatment of type 2 diabetes mellitus (p.431) in doses of 12.5 to 75 mg daily. Daily doses of 50 mg or more are given in 2 divided doses.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Glutnil; ***Fr.:*** Glutril; ***Ger.:*** Gluborid†; Glutril†; ***Switz.:*** Gluborid†; Glutril; ***Turk.:*** Glutril.

Gliclazide *(BAN, rINN)*

Gliclazida; Gliclazidum; Gliklatsidi; Gliklazid; Gliklazidas; Glyclazide; SE-1702. 1-(3-Azabicyclo[3.3.0]oct-3-yl)-3-tosylurea; 1-(3-Azabicyclo[3.3.0]oct-3-yl)-3-*p*-tolylsulphonylurea.

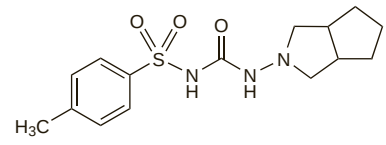
Гликлазид

$C_{15}H_{21}N_3O_3S$ = 323.4.

CAS — 21187-98-4.

ATC — A10BB09.

ATC Vet — QA10BB09.



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

Ph. Eur. 6.2 (Gliclazide). A white or almost white powder. Practically insoluble in water; slightly soluble in alcohol; sparingly soluble in acetone; freely soluble in dichloromethane.

Adverse Effects, Treatment, and Precautions

As for sulfonylureas in general, p.460.

The *BNF* suggests that gliclazide may be suitable for use in patients with renal impairment, but that careful monitoring of blood-glucose concentration is essential. UK licensed product information recommends that it should not be used in patients with severe renal impairment.

Interactions

As for sulfonylureas in general, p.461.