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.

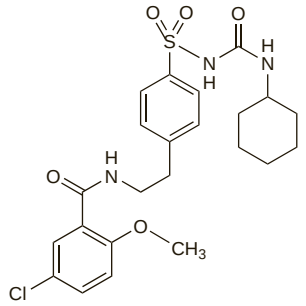
Глибенкламид

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

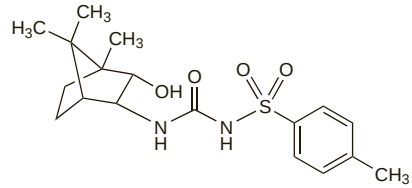
Глиборнурид

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

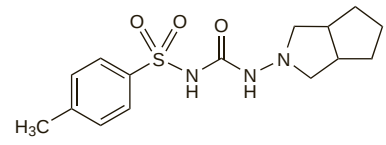
Гликлазид

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