Pharmacokinetics
Gliclazide is readily absorbed from the gastrointestinal tract. It is extensively bound to plasma proteins. The half-life is about 10 to 12 hours. Gliclazide is extensively metabolised in the liver to metabolites that have no significant hypoglycaemic activity. Metabolites and a small amount of unchanged drug are excreted in the urine.

◊ References.

1. Kobayashi K, *et al*. Pharmacokinetics of gliclazide in healthy and diabetic subjects. *J Pharm Sci* 1984; **73:** 1684–7.

Uses and Administration
Gliclazide 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 12 to 24 hours. Because its effects are less prolonged than those of chlorpropamide or glibenclamide it may be more suitable for elderly patients, who are prone to hypoglycaemia with longer-acting sulfonylureas. The usual initial dose is 40 to 80 mg daily, gradually increased, if necessary, up to 320 mg daily. Doses of more than 160 mg daily are given in 2 divided doses. A modified-release tablet is also available: the usual initial dose is 30 mg once daily, increased if necessary up to a maximum of 120 mg daily.

◊ References.

1. Palmer KJ, Brogden RN. Gliclazide: an update of its pharmacological properties and therapeutic efficacy in non-insulin-dependent diabetes mellitus. *Drugs* 1993; **46:** 92–125.
2. Mailhot J. Efficacy and safety of gliclazide in the treatment of non-insulin-dependent diabetes mellitus: a Canadian multicenter study. *Clin Ther* 1993; **15:** 1060–8.
3. Ziegler O, Drouin P. Hemobiological properties of gliclazide. *J Diabetes Complications* 1994; **8:** 235–9.
4. Jennings PE. Vascular benefits of gliclazide beyond glycemic control. *Metabolism* 2000; **49** (suppl 2): 17–20.
5. Crepaldi G, Fioretto P. Gliclazide modified release: its place in the therapeutic armamentarium. *Metabolism* 2000; **49** (suppl 2): 21–5.
6. McGavin JK, *et al*. Gliclazide modified release. *Drugs* 2002; **62:** 1357–64.

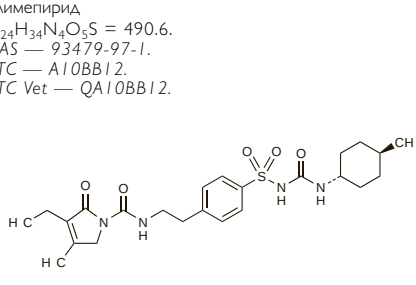
Preparations
BP 2008: Gliclazide Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Aglucide; Diamicron; Unava; ***Austral.:*** Diamicron; Glyade; Nidem; Oziclide; ***Austria:*** Diamicron; ***Belg.:*** Diamicron; Uni Diamicron; ***Braz.:*** Azukon; Diamicron; Glicaron; ***Canad.:*** Diamicron; ***Chile:*** Dianormax; ***Cz.:*** Diabrezide†; Diaprel; ***Denm.:*** Diamicron; ***Fr.:*** Diamicron; ***Ger.:*** Diamicron; ***Gr.:*** Diamicron; ***Hong Kong:*** CP-Gliz; Diamicron; Diamitex; Dianorm; Glimicron; Glucozide; Glupozide; Glyzyl; Licla; Marclazide; Nidem; Qualizide; Suclear; Sun-Glizide; ***Hung.:*** Diaprel; Gluctam; ***India:*** Diamicron; Gliza; Glizid; Glycigon; Glycinorm; Glygard; Lycazid; Semi-Glycigon; ***Indon.:*** Diamicron; Fredam; Glicab; Glidabet; Glucodex; Glucored; Glukolos; Glycafor; Linodiab; Meltika; Nufamicron; Pedab; Tiaglib; Xepabet; Zumadiac; ***Irl.:*** Diabrezide; Diaclide; Diamicron; ***Ital.:*** Cronemet; Diabrezide; Diamicron; Dramion; Galtes; Glucobloc; ***Malaysia:*** Diacron†; Diamicron; Dianid; Glimicron; Glucozide; Glyade; Medoclazide; Melicron†; Opglucon; Reclide; Sun-Glizide; ***Mex.:*** Diamicron; ***Neth.:*** Diamicron; ***NZ:*** Diamicron; Glizon; ***Philipp.:*** Clibite; Clizid; Diaclid; Diamicron; Dianorm; Glubitor; Gluconil; Glucoprime; ***Pol.:*** Diabezidum; Diabrezide; Diaprel; Diazidan; Glazide; Glinormax; Norsulin; ***Port.:*** Diamicron; ***Rus.:*** Diabest (Диабест); Diabeton (Диабетон); Diabinax (Диабинакс); Diatica (Диатика); Glucostabil (Глюкостабил); Glydiab (Глидиаб); Reclide (Реклид); ***S.Afr.:*** Diaglucide; Diamicron; Glucomed; Glycron; Glygard; Ziclin; ***Singapore:*** Diamicron; Dianorm; Glimicron; Glizide; Glucozide; Medoclazide; Melicron†; ***Spain:*** Diamicron; Uni Diamicron; ***Switz.:*** Diamicron; ***Thai.:*** Cadicon; Diabeside; Diaclaron†; Diamaze†; Diamexon; Diamicron; Dianid; Glicron; Glucocron; Glucozide; Glycon; Medoclazide; Serviclazide; ***Turk.:*** Betanorm; Diamicron; Glazid; Glumikron; Oramikron; ***UAE:*** Glyzide; ***UK:*** Diaglyk; Diamicron; ***Venez.:*** Diamicron; Glidan; Reclide†.

Multi-ingredient: ***India:*** Exermet GZ; Gliclamet; Glizid-M; Glycigon-M; Glycinorm M; Glygard M; Glyroz.

Glimepiride *(BAN, USAN, rINN)*
Glimepirid; Glimepirida; Glimépiride; Glimepiridi; Glimepiridum; Glimepiryd; Hoe-490. 1-({*p*-[2-(3-Ethyl-4-methyl-2-oxo-3-pyrroline-1-carboxamido)ethyl]phenyl}sulfonyl)-3-(*trans*-4-methylcyclohexyl)urea.

Глимепирид
$C_{24}H_{34}N_4O_5S$ = 490.6.
CAS — 93479-97-1.
ATC — A10BB12.
ATC Vet — QA10BB12.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Glimepiride). A white to almost white powder. It exhibits polymorphism. Practically insoluble in water; slightly soluble in dichloromethane; soluble in dimethylformamide; very slightly soluble in methyl alcohol.
USP 31 (Glimepiride). A white to almost white powder. Practically insoluble in water; sparingly soluble in dichloromethane; soluble in dimethylformamide; slightly soluble in methyl alcohol. It dissolves in dilute alkali hydroxides and in dilute acids. Store at a temperature not exceeding 25°.

Adverse Effects, Treatment, and Precautions
As for sulfonylureas in general, p.460. In some countries hepatic and haematological monitoring is recommended in patients receiving glimepiride; in the UK the *BNF* considers the practical value of such monitoring unproven.

Fasting. Glimepiride, given in unchanged doses but with the time of the single daily dose switched from morning to just before breaking fast after sunset, was used in Muslim patients during Ramadan without causing an increased incidence of hypoglycaemic episodes.[1]

For further advice on the management of diabetes mellitus in fasting Muslim patients during Ramadan see under Precautions of Insulin, p.448.

1. The Glimepiride in Ramadan (GLIRA) Study Group. The efficacy and safety of glimepiride in the management of type 2 diabetes in Muslim patients during Ramadan. *Diabetes Care* 2005; **28:** 421–2.

Interactions
As for sulfonylureas in general, p.461.

Pharmacokinetics
Glimepiride is completely absorbed from the gastrointestinal tract. Peak plasma concentrations occur in 2 to 3 hours, and it is highly protein bound. The drug is extensively metabolised to two main metabolites, a hydroxy derivative and a carboxy derivative. The half-life after multiple doses is about 9 hours. About 60% of a dose is eliminated in the urine and 40% in the faeces.

Uses and Administration
Glimepiride is a sulfonylurea antidiabetic (p.460). It is given orally for the treatment of type 2 diabetes mellitus (p.431). Initial doses of 1 to 2 mg daily may be increased if necessary to 4 mg daily for maintenance. The maximum recommended dose is 6 mg in the UK and 8 mg in the USA.

◊ References.

1. Langtry HD, Balfour JA. Glimepiride: a review of its use in the management of type 2 diabetes mellitus. *Drugs* 1998; **55:** 563–84.
2. Campbell RK. Glimepiride: role of a new sulfonylurea in the treatment of type 2 diabetes mellitus. *Ann Pharmacother* 1998; **32:** 1044–52.
3. McCall AL. Clinical review of glimepiride. *Expert Opin Pharmacother* 2001; **2:** 699–713.
4. Massi-Benedetti M. Glimepiride in type 2 diabetes mellitus: a review of the worldwide therapeutic experience. *Clin Ther* 2003; **25:** 799–816.
5. Weitgasser R, *et al*. Effects of glimepiride on HbA(1c) and body weight in type 2 diabetes: results of a 1.5-year follow-up study. *Diabetes Res Clin Pract* 2003; **61:** 13–19.
6. Feinbock C, *et al*. Prospective multicentre trial comparing the efficacy of, and compliance with, glimepiride or acarbose treatment in patients with type 2 diabetes not controlled with diet alone. *Diabetes Nutr Metab* 2003; **16:** 214–21.

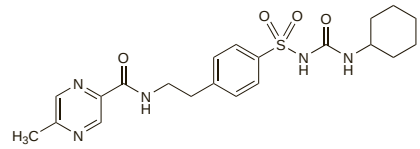
Preparations
USP 31: Glimepiride Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Adiuvan; Amaryl; Endial; Glemaz; Gluceride; Glucopirida; Islopir; Lomet; Next Step; ***Austral.:*** Amaryl; Aylide; Diapride; Dimirel; ***Austria:*** Amaryl; ***Belg.:*** Amarylle; ***Braz.:*** Amaryl; Azulix; Bioglic; Diamellitis; Glimepibal; Glimepil; Glimeprid†; Glimeran; Glimesec†; Hipomeril; ***Canad.:*** Amaryl; ***Chile:*** Amaryl; Glemaz; Glucomet; ***Cz.:*** Amarwin; Amaryl; Amyx; Apo-Glimep; Eglymad; Glemid; GlimTek; Glymexan; Melyd; Metis; Oltar; ***Denm.:*** Amaryl; ***Fin.:*** Amaryl; ***Fr.:*** Amarel; ***Ger.:*** Amaryl; Glimegamma; Glimerid; ***Gr.:*** Dialosa; Glimepiron; Glimespes; Glimexin; Gliperin; Mepirid; Penoza; Pharlecon; Saccharofar; Solosa; Sucryl; Tipo II; Toremol; ***Hong Kong:*** Amaryl; Diapride; ***Hung.:*** Amaryl; Dialosa; Glempid; GlimeWin; Glindia; Gliprex; Limeral; Meglimid; Melyd; Sintecal; ***India:*** Amaryl; Betaglim†; Diaglim; Euglim; Glimcip; Glimiprex; Glimitab; Glimulin; Glyree; Glyree M; Karmelitos; ***Indon.:*** Amadiab; Amaryl; Anpiride; Glamarol; Glimexal; Gluvas; Mapryl; Metrix; Relide; ***Irl.:*** Amaryl; ***Israel:*** Amaryl; ***Ital.:*** Amaryl; Solosa; ***Malaysia:*** Amaryl; Diapride; Glimaryl; Glimin; Glimulin; Miaryl; ***Mex.:*** Amaryl; Glupropan; Zukedib; ***Neth.:*** Amaryl; ***Norw.:*** Amaryl; ***NZ:*** Amaryl; ***Philipp.:*** Imerid; Norizec; Solosa; ***Pol.:*** Amaryl; Amyx; Avaron; Betaglid; Dianil; Glemid; Glibetic; Glibezid; Glidiamid; Glimehexal; Glimesan; Glipid; Limeral; Melyd; Oltar; Pemidal; Symglic; ***Port.:*** Amaryl; Diapiride; Glimial; Gludon; ***Rus.:*** Amaryl (Амарил); Glemaz (Глемаз); ***S.Afr.:*** Amaryl; Glamaryl; ***Singapore:*** Amaryl; Diapride; ***Spain:*** Amaryl; Roname; ***Swed.:*** Amaryl; ***Switz.:*** Amaryl; ***Thai.:*** Amaryl; ***Turk.:*** Amaryl; Diameprid; Glimax; ***UK:*** Amaryl; Niddaryl; ***USA:*** Amaryl; ***Venez.:*** Amaryl; Dimavyl; Glimerid.

Multi-ingredient: ***Cz.:*** Avaglim; Tandemact; ***Fr.:*** Avaglim; Tandemact; ***Gr.:*** Avaglim; ***Hung.:*** Avaglim; ***India:*** Betaglim M†; Exermet GM; Glimiprex MF; Glimulin-MF†; ***Indon.:*** Avandaryl; ***Mex.:*** Glimetal; ***Port.:*** Avaglim; Tandemact; ***USA:*** Avandaryl; Duetact.

Glipizide *(BAN, USAN, pINN)*
CP-28720; Glipitsidi; Glipizid; Glipizida; Glipizidas; Glipizidum; Glipizyd; Glydiazinamide; K-4024. 1-Cyclohexyl-3-{4-[2-(5-methylpyrazine-2-carboxamido)ethyl]benzenesulphonyl}urea.

Глипизид
$C_{21}H_{27}N_5O_4S$ = 445.5.
CAS — 29094-61-9.
ATC — A10BB07.
ATC Vet — QA10BB07.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US.*
Ph. Eur. 6.2 (Glipizide). A white or almost white crystalline powder. Practically insoluble in water and in alcohol; very slightly soluble in acetone and in dichloromethane. It dissolves in dilute solutions of alkali hydroxides.
USP 31 (Glipizide). Store in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions
As for sulfonylureas in general, p.460.

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

Interactions
As for sulfonylureas in general, p.461.

Antacids. *Magnesium hydroxide* and *sodium bicarbonate* have been reported to increase the rate of absorption, although not the total amount absorbed, of a dose of glipizide in healthy subjects.[1,2] No such effect was seen with *aluminium hydroxide*.[2]

1. Kivisto KT, Neuvonen PJ. Enhancement of absorption and effect of glipizide by magnesium hydroxide. *Clin Pharmacol Ther* 1991; **49:** 39–43.
2. Kivisto KT, Neuvonen PJ. Differential effects of sodium bicarbonate and aluminium hydroxide on the absorption and activity of glipizide. *Eur J Clin Pharmacol* 1991; **40:** 383–6.

Pharmacokinetics
Glipizide is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring 1 to 3 hours after a single dose. It is extensively bound to plasma proteins and has a half-life of about 2 to 4 hours. It is metabolised mainly in the liver and excreted chiefly in the urine, largely as inactive metabolites.

Uses and Administration
Glipizide 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 is 2.5 to 5 mg daily given as a single dose about 30 minutes before breakfast. Dosage may be adjusted at intervals of several days by amounts of 2.5 to 5 mg daily, to a maximum of 20 mg daily. Doses up to 40 mg daily have been used, but see below. Doses larger than 15 mg daily are given in two divided doses before meals. Modified-release formulations of glipizide are available in some countries; one such preparation (*Glucotrol XL; Pfizer, USA*) is given in doses of 5 to 10 mg daily as a single dose with breakfast.

Administration. Although glipizide may be given in doses up to a maximum of 40 mg daily, evidence for the benefits of high doses is scanty. A small study in patients with type 2 diabetes mellitus found that not only did increases in glipizide doses to more than 10 mg daily produce little or no benefit, but that the higher doses were associated with reduced rises in plasma-insulin concentrations and a lesser reduction in plasma-glucose concentrations.[1] There is, however, some evidence that glycaemic control and insulin sensitivity can be improved by the use of a modified-release rather than a conventional formulation of glipizide.[2,3]

1. Stenman S, *et al*. What is the benefit of increasing the sulfonylurea dose? *Ann Intern Med* 1993; **118:** 169–72.
2. Berelowitz M, *et al*. Comparative efficacy of once-daily controlled-release formulation of glipizide and immediate-release glipizide in patients with NIDDM. *Diabetes Care* 1994; **17:** 1460–4.
3. Leaf E, King JO. Patient outcomes after formulary conversion from immediate-release to extended-release glipizide tablets. *Am J Health-Syst Pharm* 1999; **56:** 454–6.