Preparations

BP 2008: Glipizide Tablets;
USP 31: Glipizide and Metformin Hydrochloride Tablets; Glipizide Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Minodiab; ***Austral.:*** Melizide; Minidiab; ***Austria:*** Glibenese; Minidiab; ***Belg.:*** Glibenese; Minidiab; ***Braz.:*** Glipgen†; Minidiab; ***Chile:*** Minidiab; Xiprine; ***Cz.:*** Antidiab†; Glucotrol†; Mediab†; Minidiab; ***Denm.:*** Glibenese; Mindiab; ***Fin.:*** Apamid†; Glibenese; Melizid; Mindiab; ***Fr.:*** Glibenese; Minidiab; Ozidia; ***Gr.:*** Glibenese; Minodiab†; ***Hong Kong:*** Diasef; Glucotrol; Minidiab; Sunglucon; ***Hung.:*** Minidiab; ***India:*** Diaglip; Glez; Glide; Glipicontin†; Glucolip; Glynase; Glyzip; ***Indon.:*** Aldiab; Glucotrol; Glyzid; ***Irl.:*** Glibenese; ***Israel:*** Gluco-Rite; ***Ital.:*** Minidiab; ***Malaysia:*** Dibizide†; Dipazide; Glix; Melizide; Minidiab; ***Mex.:*** Glupitel†; Luditec; Minodiab; Pigloss; Singloben; ***Neth.:*** Glibenese†; ***Norw.:*** Apamid; Mindiab; ***NZ:*** Glipid†; Minidiab; ***Philipp.:*** Glix; Minidiab; ***Pol.:*** Antidiab; Glibenese; ***Port.:*** Minidiab; ***Rus.:*** Glibenese (Глибенез); Minidiab (Минидиаб)†; ***S.Afr.:*** Minidiab; ***Singapore:*** Beapizide; Diactin; Diasef; Melizide; Minidiab; ***Spain:*** Glibenese†; Minodiab; ***Swed.:*** Apamid†; Glipiscand†; Mindiab; ***Switz.:*** Glibenese; ***Thai.:*** Apamid†; Depizide; Diasef; Dipazide; Gipzide; Glipimed; Glizide; Glucodiab; Glygen; GP-Zide; Melizide; Minibit; Minidiab; Namedia; Pezide; ***Turk.:*** Glucotrol; Minidiab; ***UK:*** Glibenese; Minodiab; ***USA:*** Glucotrol; ***Venez.:*** Minidiab.

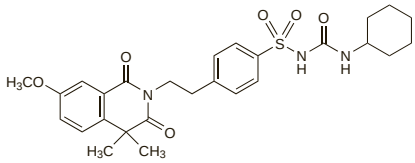
Multi-ingredient: ***India:*** Diaglip M; Metaglez; ***USA:*** Metaglip.

Gliquidone *(BAN, rINN)*

ARDF-26; Glikidon; Glikidoni; Gliquidona; Gliquidonum. 1-Cyclohexyl-3-{4-[2-(3,4-dihydro-7-methoxy-4,4-dimethyl-1,3-dioxo-2(1*H*)-isoquinolyl)ethyl]benzenesulphonyl}urea.

Гликвидон

$C_{27}H_{33}N_3O_6S$ = 527.6.
CAS — 33342-05-1.
ATC — A10BB08.
ATC Vet — QA10BB08.



Pharmacopoeias. In *Br.* and *Chin.*
BP 2008 (Gliquidone). A white or almost white powder. Practically insoluble in water; slightly soluble in alcohol and in methyl alcohol; soluble in acetone; freely soluble in dimethylformamide.

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

Interactions
As for sulfonylureas in general, p.461.

Pharmacokinetics
Gliquidone is readily absorbed from the gastrointestinal tract. It is extensively bound to plasma proteins and has a half-life of about 1.5 hours. It is extensively metabolised in the liver, the metabolites having no significant hypoglycaemic effect, and is eliminated chiefly in the faeces via the bile; only about 5% of a dose is excreted in the urine.

Uses and Administration
Gliquidone is a sulfonylurea antidiabetic (p.460). It has been given orally in the treatment of type 2 diabetes mellitus (p.431) in a usual initial dosage of 15 mg daily given as a single dose up to 30 minutes before breakfast. Dosage may be adjusted by increments of 15 mg to a usual dose of 45 to 60 mg daily in 2 or 3 unequally divided doses, the largest dose being taken in the morning with breakfast. Single doses above 60 mg and daily doses above 180 mg are not recommended.

Preparations

BP 2008: Gliquidone Tablets.

Proprietary Preparations (details are given in Part 3)

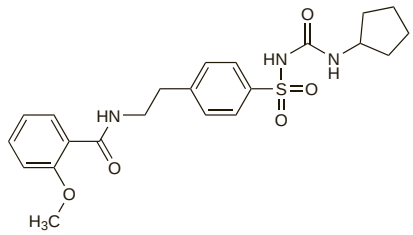
Austria: Glurenorm; ***Belg.:*** Glurenorm; ***Cz.:*** Glurenorm; ***Ger.:*** Glurenorm; ***Gr.:*** Devotan; ***Hung.:*** Glurenorm; ***Indon.:*** Glurenorm; ***Ital.:*** Glurenor; ***Pol.:*** Glurenorm; ***Port.:*** Glurenor†; ***Rus.:*** Glurenorm (Глюренорм); ***Spain:*** Glurenor; ***Thai.:*** Glurenor; ***Turk.:*** Glurenorm; ***UK:*** Glurenorm†.

Glisentide *(rINN)*

Glipentide; Glisentida; Glisentidum. 1-Cyclopentyl-3-[*p*-(2-*o*-anisamidoethyl)benzenesulphonyl]urea.

Глизентид

$C_{22}H_{27}N_3O_5S$ = 445.5.
CAS — 32797-92-5.



Profile
Glisentide is a sulfonylurea antidiabetic (p.460). It is given orally in the treatment of type 2 diabetes mellitus (p.431) in doses of 2.5 to 20 mg daily.

Preparations

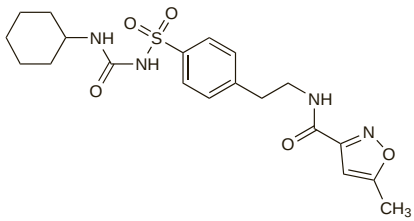
Proprietary Preparations (details are given in Part 3)
Spain: Staticum.

Glisolamide *(rINN)*

Glisolamida; Glisolamidum. 1-Cyclohexyl-3-{*p*-[2-(5-methylisoxazole-3-carboxamido)ethyl]benzenesulphonyl}urea.

Глизоламид

$C_{20}H_{26}N_4O_5S$ = 434.5.
CAS — 24477-37-0.



Profile
Glisolamide is a sulfonylurea antidiabetic (p.460). It has been given in the treatment of type 2 diabetes mellitus.

Preparations

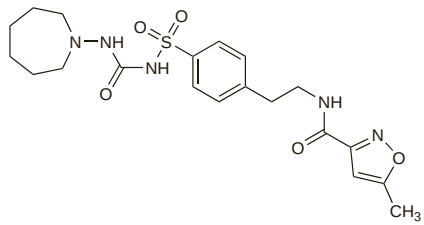
Proprietary Preparations (details are given in Part 3)
Ital.: Diabenor†.

Glisoxepide *(BAN, rINN)*

Bay-b-4231; FBB-4231; Glisoxepid; Glisoxepida; Glisoxépide; Glisoxepidum; RP-22410. 1-(Perhydroazepin-1-yl)-3-{4-[2-(5-methylisoxazole-3-carboxamido)ethyl]benzenesulphonyl}urea.

Глизоксепид

$C_{20}H_{27}N_5O_5S$ = 449.5.
CAS — 25046-79-1.
ATC — A10BB11.
ATC Vet — QA10BB11.



Profile
Glisoxepide is a sulfonylurea antidiabetic (p.460). It has been given in the treatment of type 2 diabetes mellitus.

Preparations

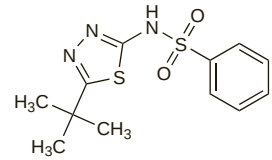
Proprietary Preparations (details are given in Part 3)
Austria: Pro-Diaban†.

Glybuzole *(rINN)*

AN-1324; Désaglybuzole; Glibuzol; Glybuzolum; RP-7891. *N*-(5-*tert*-Butyl-1,3,4-thiadiazol-2-yl)benzenesulphonamide.

Глибузол

$C_{12}H_{15}N_3O_2S_2$ = 297.4.
CAS — 1492-02-0.



Profile
Glybuzole is an oral antidiabetic with a structure distinct from that of the sulfonylureas, biguanides, or sulfonamidopyrimidines.

Preparations

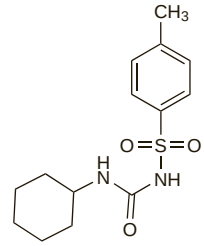
Proprietary Preparations (details are given in Part 3)
Jpn: Gludiase.

Glycyclamide *(rINN)*

Gliciclamida; Gliciclamide; Glycyclamidum; K-38; K-386; Tolcyclamide. 1-Cyclohexyl-3-tosylurea; 1-Cyclohexyl-3-*p*-tolylsulphonylurea.

Глицикламид

$C_{14}H_{20}N_2O_3S$ = 296.4.
CAS — 664-95-9.



Profile
Glycyclamide is a sulfonylurea antidiabetic (p.460). It is given by mouth in the treatment of type 2 diabetes mellitus.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Diaborale.

Guar Gum

Cyamopsidis seminis pulvis; E412; Goma guar; Guar; Guar Flour; Guar Galactomannan; Guar, galactomannane du; Guar galactomannanum; Guar galaktomanan; Guar galaktomannan; Guaras; Guárbab galaktomannán; Guárbabmag-por; Guargalaktomannaani; Guargalaktomannan; Guaro galaktomananas; Jaguar Gum.

CAS — 9000-30-0.
ATC — A10BX01.
ATC Vet — QA10BX01.

Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF.*
Ph. Eur. 6.2 (Guar). Guar is obtained by grinding the endosperms of the seeds of *Cyamopsis tetragonolobus*. It consists mainly of guar galactomannan. Guar is a white or almost white powder, yielding a mucilage of variable viscosity when dissolved in water. Practically insoluble in alcohol.
Ph. Eur. 6.2 (Guar Galactomannan). A yellowish-white powder. It is soluble in cold and hot water; practically insoluble in organic solvents. Its main components are polysaccharides composed of D-galactose and D-mannose at molecular ratios of 1:1.4 to 1:2. The molecules consist of a linear main chain of β-(1→4)-glycosidically linked mannopyranoses and single α-(1→6)-glycosidically linked galactopyranoses.
USNF 26 (Guar Gum). A gum obtained from the ground endosperms of *Cyamopsis tetragonolobus* (Leguminosae). It consists chiefly of a high-molecular-weight hydrocolloidal polysaccharide, a galactomannan, composed of galactan and mannan units combined through glycosidic linkages. It is a white to yellowish-white, practically odourless, powder. Dispersible in hot or cold water forming a colloidal solution.

Adverse Effects and Precautions

Guar gum can cause gastrointestinal disturbance with flatulence, diarrhoea, or nausea, particularly at the start of treatment.

Because guar gum swells on contact with liquid it should always be washed down carefully with water and should not be taken immediately before going to bed. It should not be used in patients with dysphagia, oesophageal disease, or intestinal obstruction.

Interactions

Guar gum may retard the absorption of other drugs; where this is likely to pose a problem the other drug should be taken at least an hour before guar gum.

Uses and Administration

Guar gum is used in diabetes mellitus (p.431) as an adjunct to treatment with diet, insulin, or oral antidiabetics since it results in some reduction in both postprandial and fasting blood-glucose concentrations. It is given with or immediately before meals in doses of 5 g usually 3 times daily. Adverse gastrointestinal effects may be reduced by using a lower initial dose of 5 g once daily before breakfast for 1 week, then increasing to 5 g twice daily, then 3 times daily, as required. Each dose of guar gum granules should be taken stirred in about 200 mL of a cold drink. Alternatively it can be sprinkled over or mixed with food which must be taken with about 200 mL of fluid.

Guar gum is also used to slow gastric emptying in some patients with the dumping syndrome (p.1695). It is also used as an adjunct in the treatment of hyperlipidaemias.

Guar gum is also used as a thickening and suspending agent, and as a tablet binder. It has been incorporated into processed foods.

◊ Guar gum is an example of a soluble fibre.[1] On contact with water it forms a highly viscous gel, the viscosity of which varies with such factors as its plant source or the form in which it is given.[2]

Fibres such as guar gum reduce postprandial and fasting blood-glucose concentrations as well as plasma-insulin concentrations in healthy subjects and diabetic patients.[1,3,4] Such reductions in blood-glucose concentrations and in glycosylated haemoglobin have been demonstrated in both type 1 and type 2 **diabetes,** but they have generally been small.[3] Possible mechanisms for these effects of guar gum include a delay in gastric emptying,[1,3-5] decreased small-bowel motility,[1,4] decreased glucose absorption resulting from increased viscosity of the contents of the gastrointestinal tract,[1,3] or inhibition of gastrointestinal hormones.[3]

Guar gum also lowers serum total cholesterol and low-density-lipoprotein (LDL) cholesterol concentrations; high-density-lipoprotein (HDL) cholesterol and triglyceride concentrations appear to be unaffected.[4] The most likely mechanism is binding of bile acids, reducing their enterohepatic circulation in a similar way to bile-acid sequestrants.[3,4] When used alone in patients with **hypercholesterolaemia** guar gum has generally produced a modest reduction in plasma-cholesterol and LDL-cholesterol concentrations although some studies have been unable to demonstrate an effect. A few studies have suggested that the cholesterol-lowering effect is attenuated after 8 to 12 weeks of treatment but a long-term study observed a 17% decrease in total serum cholesterol that was maintained for 24 months.[6] Some studies have shown further reductions in cholesterol and LDL-cholesterol concentrations on addition of guar gum to therapy with other lipid regulating drugs.[4] The usual treatment of hyperlipidaemias is discussed on p.1169.

There have been suggestions that guar gum reduces appetite by promoting a feeling of fullness, but a meta-analysis has indicated that it is not effective for reducing body-weight.[7] Products containing guar gum have, however, been promoted as **slimming aids**. Their use cannot be advocated because of the risk of tablets swelling before reaching the stomach and causing oesophageal obstruction.

1. Hockaday TDR. Fibre in the management of diabetes 1: natural fibre useful as part of total dietary prescription. *BMJ* 1990; **300:** 1334–6.
2. Ellis PR, *et al.* Guar gum: the importance of reporting data on its physico-chemical properties. *Diabet Med* 1986; **3:** 490–1.
3. Anonymous. Guar gum: of help to diabetics? *Drug Ther Bull* 1987; **25:** 65–7.
4. Todd PA, *et al.* Guar gum: a review of its pharmacological properties, and use as a dietary adjunct in hypercholesterolaemia. *Drugs* 1990; **39:** 917–28.
5. Tattersall R, Mansell P. Fibre in the management of diabetes 2: benefits of fibre itself are uncertain. *BMJ* 1990; **300:** 1336–7.
6. Salenius J-P, *et al.* Long term effects of guar gum on lipid metabolism after carotid endarterectomy. *BMJ* 1995; **310:** 95–6.
7. Pittler MH, Ernst E. Guar gum for body weight reduction: meta-analysis of randomized trials. *Am J Med* 2001; **110:** 724–30.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Regudig†; ***Austral.:*** Benefiber†; ***Braz.:*** Benefiber†; Biofiber†; ***Fin.:*** Guarem; ***Ger.:*** Figur-Verlan; Guar Verlan; ***Hong Kong:*** Guarem†; ***Irl.:*** Guarem†; ***Ital.:*** Novafibra; ***NZ:*** Guarcol; ***Spain:*** Fibraguar; Plantaguar; ***Switz.:*** Leiguar; ***UK:*** Resource Benefiber; ***USA:*** Benefiber.

Multi-ingredient: ***Fr.:*** Carres Parapsyllium; Moxydar; Mucipulgite; Mulkine; Seroxydar; ***Ital.:*** Cruscasohn; Resource Gelificata; ***Switz.:*** Mucipulgite†.

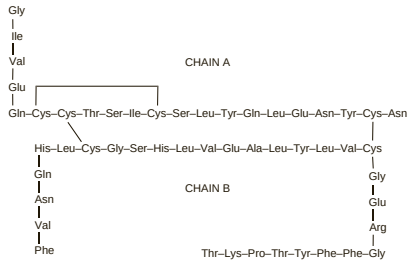
Insulin ⊗

Insuliini; Insülin; Insulina; Insuline; Insulinin; Insulinum.

CAS — 9004-10-8 (insulin; neutral insulin); 11070-73-8 (bovine insulin); 12584-58-6 (porcine insulin); 11061-68-0 (human insulin); 8063-29-4 (biphasic insulin); 9004-21-1 (globin zinc insulin); 68859-20-1 (insulin argine); 8049-62-5 (insulin zinc suspensions); 53027-39-7 (isophane insulin); 9004-17-5 (protamine zinc insulin); 116094-23-6 (insulin aspart); 9004-12-0 (dalanated insulin); 51798-72-2 (bovine insulin defalan); 11091-62-6 (porcine insulin defalan); 160337-95-1 (insulin glargine); 133107-64-9 (insulin lispro).

ATC — A10AB01 (human); A10AB02 (beef); A10AB03 (pork); A10AB04 (lispro); A10AB05 (aspart); A10AB06 (glulisine); A10AC01 (human); A10AC02 (beef); A10AC03 (pork); A10AC04 (lispro); A10AE01 (human); A10AE02 (beef); A10AE03 (pork); A10AE04 (glargine); A10AE05 (detemir).

ATC Vet — QA10AB01 (human); QA10AB02 (beef); QA10AB03 (pork); QA10AB04 (lispro); QA10AB05 (aspart); QA10AB06 (glulisine); QA10AC01 (human); QA10AC02 (beef); QA10AC03 (pork); QA10AC04 (lispro); QA10AD01 (human); QA10AD02 (beef); QA10AD03 (pork); QA10AD04 (lispro); QA10AD05 (aspart); QA10AE01 (human); QA10AE02 (beef); QA10AE03 (pork); QA10AE04 (glargine); QA10AE05 (detemir); QA10AF01 (human).



(human)

Pharmacopoeias. Most pharmacopoeias have monographs for insulin and a variety of insulin preparations.

Ph. Eur. 6.2 (Insulin, Bovine). The natural antidiabetic principle obtained from beef pancreas and purified. A white or almost white powder. Practically insoluble in water and in dehydrated alcohol. It dissolves in dilute mineral acids and, with decomposition, in dilute solutions of alkali hydroxides. Store in airtight containers. Protect from light. It should be stored at –20° until released by the manufacturer. When thawed, insulin may be stored at 2° to 8° and used for manufacturing purposes within a short period of time. To avoid absorption of humidity from the air during weighing, the insulin must be at room temperature.

Ph. Eur. 6.2 (Insulin, Porcine). The natural antidiabetic principle obtained from pork pancreas and purified. A white or almost white powder. Practically insoluble in water and in dehydrated alcohol. It dissolves in dilute mineral acids and, with decomposition, in dilute solutions of alkali hydroxides. Store in airtight containers. Protect from light. It should be stored at –20° until released by the manufacturer. When thawed, insulin may be stored at 2° to 8° and used for manufacturing purposes within a short period of time. To avoid absorption of humidity from the air during weighing, the insulin must be at room temperature.

Ph. Eur. 6.2 (Insulin, Human). A protein having the structure of the antidiabetic hormone produced by the human pancreas. It is produced either by enzymatic modification and suitable purification of insulin obtained from the pancreas of the pig or by a method based on recombinant DNA (rDNA) technology. A white or almost white powder. Practically insoluble in water and in alcohol. It dissolves in dilute mineral acids and, with decomposition, in dilute solutions of alkali hydroxides. Store in airtight containers. Protect from light. It should be stored at or below –18° or below until released by the manufacturer. When thawed, insulin is stored at 2° to 8° and used for manufacturing preparations within a short period of time. To avoid absorption of humidity from the air during weighing, the insulin must be at room temperature.

Ph. Eur. 6.2 (Insulin Aspart; Insulinum Aspartum). It is a 2-chain peptide containing 51 amino acids. The A-chain is composed of 21 amino acids and the B-chain is composed of 30 amino acids. It is identical in primary structure to human insulin, except that it has aspartic acid instead of proline at position 28 of the B-chain. As in human insulin, insulin aspart contains 2 interchain disulfide bonds and 1 intrachain disulfide bond. It is produced by a method based on recombinant DNA (rDNA) technology. A white or almost white powder. Practically insoluble in aqueous solutions with a pH around 5.1. In aqueous solutions below pH 3.5 or above pH 6.5, the solubility is greater than or equal to 25 mg/mL. Store in airtight containers. Protect from light. It should be stored at or below –18° until released by the manufacturer. When thawed, insulin aspart may be stored at 2° to 8° and used for manufacturing purposes within a short period of time. To avoid absorption of humidity from the air during weighing, insulin aspart must be at room temperature before opening the container.

Ph. Eur. 6.2 (Insulin Lispro; Insulinum Lisprum). It is a 2-chain peptide containing 51 amino acids. The A-chain is composed of 21 amino acids and the B-chain is composed of 30 amino acids. It is identical in primary structure to human insulin, only differing in amino acid sequence at positions 28 and 29 of the B-chain. Human insulin is Pro(B28), Lys(B29), whereas insulin lispro is Lys(B28), Pro(B29). As in human insulin, insulin lispro contains 2 interchain disulfide bonds and 1 intrachain disulfide bond. It is produced by a method based on recombinant DNA (rDNA) technology. A white or almost white powder. Practically insoluble in water and in alcohol. It dissolves in dilute mineral acids and with decomposition in dilute solutions of alkali hydroxides. Store in airtight containers. Protect from light. It should be stored at or below –18°. When thawed, insulin lispro is used for manufacturing purposes within a short period of time. To avoid absorption of humidity from the air during weighing, insulin aspart must be at room temperature before opening the container.

USP 31 (Insulin). A protein that affects the metabolism of glucose obtained from the pancreas of healthy bovine or porcine animals, or both, used for food by humans. White or practically white crystals. Soluble in solutions of dilute acids and alkalis. Store in airtight containers. Protect from light. It should be stored at –10° to –25°.

USP 31 (Insulin Human). A protein corresponding to the active principle elaborated in the human pancreas that affects the metabolism of carbohydrate (particularly glucose), fat, and protein. It is derived by enzymatic modification of insulin from pork pancreas in order to change its amino acid sequence appropriately, or produced by microbial synthesis via a recombinant DNA process. Store in airtight containers. Protect from light. It should be stored at –10° to –25°.

USP 31 (Insulin Lispro). Insulin Lispro is identical in structure to Insulin Human, except that it has lysine and proline at positions 28 and 29, respectively, of chain B, whereas this sequence is reversed in Insulin Human. It is produced by microbial synthesis via a recombinant DNA process. White or practically white crystals. Soluble in solutions of dilute acids and alkalis. Store in airtight containers. Protect from light. It should be stored at –10° to –25°.

Definitions and Terminology

Insulin is a hormone produced by the beta cells of the islets of Langerhans of the pancreas and consists of 2 chains of amino acids, the A and B chains, connected by 2 disulfide bridges. Insulin produced by different species conforms to the same basic structure but has different sequences of amino acids in the chains. **Porcine insulin** ($C_{256}H_{381}N_{65}O_{76}S_6$ = 5777.5) differs from **human insulin** ($C_{257}H_{383}N_{65}O_{77}S_6$ = 5807.6) in only one amino acid in the B chain, whereas **bovine insulin** ($C_{254}H_{377}N_{65}O_{75}S_6$ = 5733.5) differs from human insulin not only in this same amino acid in the B chain but also in 2 amino acids in the A chain.

The precursor of insulin in the pancreas is proinsulin which is a single polypeptide chain incorporating both the A and B chains of insulin connected by a peptide termed the C-peptide (or connecting-peptide). Although the insulins of various species may be similar in composition the proinsulins are not, in that the sequence and number of amino acids in the C-peptide may vary considerably.

Early commercial insulins were obtained by extraction from bovine or porcine or mixed bovine and porcine pancreases and were purified by recrystallisation only.