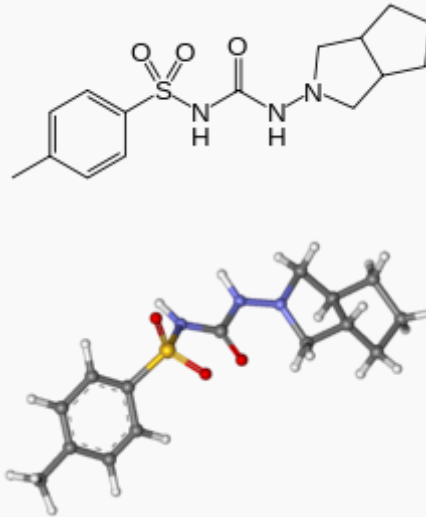


Gliclazide

Gliclazide



Systematic (IUPAC) name

N-(hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-ylcarbamoyl)-4-methylbenzenesulfonamide

Clinical data

[AHFS/Drugs.com](#)

[Micromedex Detailed Consumer Information](#)

[Legal status](#)

?

Pharmacokinetic data

[Half-life](#)

10.4 hours

Identifiers

[CAS number](#)

[21187-98-4](#)

[ATC code](#)

[A10BB09](#)

[PubChem](#)

[CID 3475](#)

[DrugBank](#)

[DB01120](#)

ChemSpider	3356
UNII	G4PX8C4HKV
KEGG	D01599
ChEBI	CHEBI:31654
ChEMBL	CHEMBL427216
Chemical data	
Formula	C₁₅H₂₁N₃O₃S
Mol. mass	323.412 g/mol
SMILES	<ul style="list-style-type: none"> <chem>O=S(=O)(c1ccc(cc1)C)NC(=O)NN3CC2CCCC2C3</chem>
InChI	<p>InChI=1S/C15H21N3O3S/c1-11-5-7-14(8-6-11)22(20,21)17-15(19)16-18-9-12-3-2-4-13(12)10-18/h5-8,12-13H,2-4,9-10H2,1H3,(H2,16,17,19)</p> <p>Key:BOVGTQGAOIONJV-UHFFFAOYSA-N</p>

Gliclazide is an oral hypoglycemic ([anti-diabetic drug](#)) and is classified as a [sulfonylurea](#). Its classification has been ambiguous, as literature uses it as both a first- generation^[1] and second-generation^[2] sulfonylurea. Gliclazide was shown to protect human pancreatic beta-cells from hyperglycemia-induced [apoptosis](#).^[3] It was also shown to have an antiatherogenic effect (preventing accumulation of fat in arteries) in type 2 diabetes.^[4]

Form and composition

Each immediate-release tablet contains 80 mg. Modified release formulations contain 30 mg and 60 mg of gliclazide.

Indication

Gliclazide is used for control of hyperglycemia in gliclazide-responsive [diabetes mellitus](#) of stable, mild, non-[ketosis](#) prone, type 2 diabetes. It is used when diabetes cannot be controlled by proper dietary management and exercise or when insulin therapy is not appropriate. National Kidney Foundation (2012 Update) claims that Gliclazide doesn't requires dosage uptitration even in end stage Kidney disease.

Mode of action

Gliclazide selectively binds to sulfonylurea receptors (SUR-1) on the surface of the pancreatic beta-cells. It was shown to provide cardiovascular protection as it does not bind to sulfonylurea receptors (SUR-2A) in the heart.^[6] This binding effectively closes the K⁺ ion channels. This decreases the efflux of potassium from the cell which leads to the depolarization of the cell. This causes voltage dependent Ca⁺⁺ ion channels to open increasing the Ca⁺⁺ influx. The calcium can then bind to and activate calmodulin which in turn leads to exocytosis of insulin vesicles leading to insulin release.

Dosage

The dosage for the 80 mg formulation is 40 to 320 mg daily in two divided doses, while the 30 mg and 60 mg modified release formulation may be given at a dose of 30 to 120 mg once daily at breakfast.

Properties

Water Solubility = 0.027 mg/L^[6]

- Hypoglycemic sulfonylurea, restoring first peak of insulin secretion, increasing insulin sensitivity.
- Glycemia-independent hemovascular effects, antioxidant effect.
- No active circulating metabolites.

Contraindications

- Type 1 diabetes
- Hypersensitivity to sulfonylureas
- Severe renal or hepatic failure
- Pregnancy and lactation
- Miconazole coprescription

Metabolism

Gliclazide undergoes extensive metabolism to several inactive metabolites in humans, mainly methylhydroxygliclazide and carboxygliclazide. CYP2C9 is involved in the formation of hydroxygliclazide in human liver microsomes and in a panel of recombinant human P450s in vitro.^{[7][8]} But the pharmacokinetics of gliclazide MR are affected mainly by CYP2C19 genetic polymorphism instead of CYP2C9 genetic polymorphism.^{[9][10]}

Interactions

Hyperglycemic action may be caused by danazol, chlorpromazine, glucocorticoids, progestogens, or β -2 agonists. Its hypoglycemic action may be potentiated by phenylbutazone, alcohol, fluconazole, β -blockers, and possibly ACE inhibitors. It has been found that rifampin increases gliclazide metabolism in humans in vivo.^[11]

Adverse effects

- Hypoglycemia - while it was shown to have the same efficacy as glimepiride, one of the newer sulfonylureas, the European GUIDE study has shown that it has approximately 50% fewer confirmed hypoglycaemic episodes in comparison with glimepiride.^[12]
- Gastrointestinal disturbance (reported)
- Skin reactions (rare)
- Hematological disorders (rare)
- Hepatic enzyme rises (exceptional)

Overdosage

Gliclazide overdose may cause severe hypoglycemia, requiring urgent administration of glucose by IV and monitoring.

References

1. [▲]Ballagi-Pordány, György; Kőszeghy, Anna; Koltai, Mária-Zsófia; Arányi, Zoltán; Pogátsa, Gábor (1990). "Divergent cardiac effects of the first and second generation hypoglycemic sulfonylurea compounds". *Diabetes Research and Clinical Practice* 8 (2): 109–14. doi:10.1016/0168-8227(90)90020-T. PMID 2106423.
2. [▲]Shimoyama, Tatsuhiro; Yamaguchi, Shinya; Takahashi, Kazuto; Katsuta, Hidenori; Ito, Eisuke; Seki, Hiroyuki; Ushikawa, Kenji; Katahira, Hiroshi et al. (2006). "Gliclazide protects 3T3L1 adipocytes against insulin resistance induced by hydrogen peroxide with restoration of GLUT4 translocation". *Metabolism* 55 (6): 722–30. doi:10.1016/j.metabol.2006.01.019. PMID 16713429.
3. [▲]Del Guerra, S; Gruppillo, M; Masini, M; Lupi, R; Bugliani, M; Torri, S; Boggi, U; Del Chiaro, M et al. (2007). "Gliclazide protects human islet beta-cells from apoptosis induced by intermittent high glucose". *Diabetes/Metabolism Research and Reviews* 23 (3): 234–8. doi:10.1002/dmrr.680. PMID 16952202.
4. [▲]Katakami, N.; Yamasaki, Y.; Hayaishi-Okano, R.; Ohtoshi, K.; Kaneto, H.; Matsuhisa, M.; Kosugi, K.; Hori, M. (2004). "Metformin or gliclazide, rather than glibenclamide, attenuate progression of carotid intima-media thickness in subjects with type 2 diabetes". *Diabetologia* 47 (11): 1906–13. doi:10.1007/s00125-004-1547-8. PMID 15565373.
5. [▲]Lawrence, C. L.; Proks, P.; Rodrigo, G. C.; Jones, P.; Hayabuchi, Y.; Standen, N. B.; Ashcroft, F. M. (2001). "Gliclazide produces high-affinity block of K ATP channels in mouse isolated pancreatic beta cells but not rat heart or arterial smooth muscle cells". *Diabetologia* 44 (8): 1019–25. doi:10.1007/s001250100595. PMID 11484080.
6. [▲]Gopal Venkatesh Shavi et al. Enhanced dissolution and bioavailability of gliclazide using solid dispersion techniques; *International Journal of Drug Delivery* 2 (2010) 49-57
7. [▲]Rieutord, A; Stupans, I; Shenfield, GM; Gross, AS (1995). "Gliclazide hydroxylation by rat liver microsomes". *Xenobiotica* 25 (12): 1345–54. doi:10.3109/00498259509061922. PMID 8719909.
8. [▲]Elliot, David J.; Lewis, Benjamin C.; Gillam, Elizabeth M. J.; Birkett, Donald J.; Gross, Annette S.; Miners, John O.; Miners, JO (2007). "Identification of the human cytochromes P450 catalysing the rate-limiting pathways of gliclazide elimination". *British Journal of Clinical Pharmacology* 64 (4): 450–7. doi:10.1111/j.1365-2125.2007.02943.x. PMC 2048545. PMID 17517049.
9. [▲]Zhang, Yifan; Si, Dayong; Chen, Xiaoyan; Lin, Nan; Guo, Yingjie; Zhou, Hui; Zhong, Dafang (2007). "Influence of CYP2C9 and CYP2C19 genetic polymorphisms on pharmacokinetics of gliclazide MR in Chinese subjects". *British Journal of Clinical Pharmacology* 64(1): 67–74. doi:10.1111/j.1365-2125.2007.02846.x. PMC 2000619. PMID 17298483.
10. [▲]Xu, H; Williams, K M; Liauw, W S; Murray, M; Day, R O; McLachlan, A J (2009). "Effects of St John's wort and CYP2C9 genotype on the pharmacokinetics and pharmacodynamics of gliclazide". *British Journal of Pharmacology* 153 (7): 1579–86. doi:10.1038/sj.bjp.0707685. PMC 2437900. PMID 18204476.
11. [▲]Park, J; Kim, KA; Park, PW; Park, CW; Shin, JG (2003). "Effect of rifampin on the pharmacokinetics and pharmacodynamics of gliclazide". *Clinical Pharmacology & Therapeutics* 74 (4): 334–40. doi:10.1016/S0009-9236(03)00221-2. PMID 14534520.
12. [▲]Schemthäner, G.; Grimaldi, A.; Di Mario, U.; Drzewoski, J.; Kempler, P.; Kvapil, M.; Novials, A.; Rotliers, R. et al. (2004). "GUIDE study: Double-blind comparison of once-daily gliclazide MR and glimepiride in type 2 diabetic patients". *European Journal of Clinical Investigation* 34 (8): 535–42. doi:10.1111/j.1365-2362.2004.01361.x. PMID 15305887.