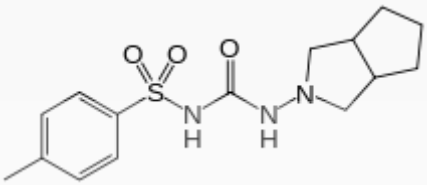
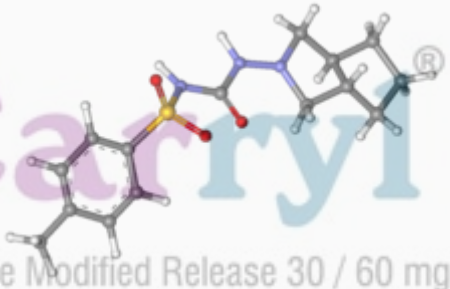
# Gliclazide

**Gliclazide**







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|---|---|
| **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 |

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|---|---|
| **ChemSpider** | 3356 |
| **UNII** | G4PX8C4HKV |
| **KEGG** | D01599 |
| **ChEBI** | CHEBI:31654 |
| **ChEMBL** | CHEMBL427216 |
| **Chemical data** | |
| **Formula** | $C_{15}H_{21}N_3O_3S$ |
| **Mol. mass** | 323.412 g/mol |
| **SMILES** | • O=S(=O)(c1ccc(cc1)C)NC(=O)NN3CC2CCCC2C3 |
| **InChI** | 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)<br>Key:BOVGTQGAOIONJV-UHFFFAOYSA-N |



**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.[5] 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 exocystosis 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 hydroxygliclazde in human liver microsomes and in a panel of recombinant human P450sin 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 sulfoylureas, 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


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