**DRUG PROFILE**

**Hydrochlorothiazide**

**Chemical name**: 6-chloro-1,1-dioxo-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide

**Molecular weight**: 297.7

**Molecular formula**: C_7H_8ClN_3O_4S_2

**Description**: White or almost white, crystalline powder

**Solubility**: Very slightly soluble in water, soluble in acetone, sparingly soluble in ethanol (96 percent). It dissolves in dilute solutions of alkali hydroxides

**Melting point**: 273-275 °C

**Category**: Thiazide diuretic

**pKa**: 7.9

**Mechanism of action**: Thiazide diuretic, inhibits water reabsorption in the nephron by inhibiting the sodium chloride symporter in the distal convoluted tubule, which is responsible for 5% of total sodium reabsorption. Normally, the sodium chloride symporter transports sodium and chloride from the lumen into the epithelial cell lining the distal convoluted tubule. The energy for this is provided by a sodium gradient established by sodium potassium ATPase on the basolateral membrane. Once sodium has entered the cell, it is transported out into the basolateral interstitium via the sodium potassium ATPase, causing an increase in the osmolarity of the interstitium, thereby establishing an osmotic gradient for water reabsorption. By blocking the sodium chloride
symporter, hydrochlorothiazide effectively reduces the osmotic gradient and water reabsorption throughout the nephron

Amlodipine besylate

![Chemical structure of Amlodipine besylate](attachment:amlodipine_besylate.png)

**Chemical name**: (RS)-3-ethyl 5-methyl 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

**Molecular weight**: 408.87

**Molecular formula**: C\textsubscript{20}H\textsubscript{25}ClN\textsubscript{2}O\textsubscript{5}

**Description**: A white or almost white crystalline powder

**Solubility**: Slightly soluble in water, freely soluble in methanol, sparingly soluble in ethanol, slightly soluble in 2-propanol

**Melting point**: 178-179 °C

**Category**: Antihypertensive (Calcium channel blocker)

**pKa**: 8.6

**Mechanism of action**: Amlodipine decreases arterial smooth muscle contractility and subsequent vasoconstriction by inhibiting the influx of calcium ions. Inhibition of the initial influx of calcium decreases the contractile activity of arterial smooth muscle cells and results in vasodilation. The vasodilatory effects of amlodipine result in an overall decrease in blood pressure. It is a long-acting CCB that may be used to treat mild to
moderate essential hypertension and exertion-related angina (chronic stable angina). Another possible mechanism is that amlodipine inhibits vascular smooth muscle carbonic anhydrase I activity causing cellular pH increases which may be involved in regulating intracellular calcium influx through calcium channels.

**Telmisartan**

![Telmisartan molecular structure]

**Chemical name**: 2-(4-[[4-methyl-6-(1-methyl-1H-1,3-benzodiazol-2-yl)-2-propyl-1H-1,3-benzodiazol-1-yl]methyl]phenyl)benzoic acid

**Molecular weight**: 514.6

**Molecular formula**: C\textsubscript{33}H\textsubscript{30}N\textsubscript{4}O\textsubscript{2}

**Description**: A white or almost white crystalline powder

**Solubility**: Insoluble in water, soluble in chloroform, slightly soluble in methanol and very slightly soluble in 96% alcohol

**Melting point**: 261-263 °C

**Category**: Antihypertensive (ARBs)

**pKa**: 3.5, 4.1, and 6.0

**Mechanism of action**: 

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Telmisartan interferes with the binding of angiotensin II to the angiotensin II AT₁-receptor by binding reversibly and selectively to the receptors in vascular smooth muscle and the adrenal gland. As angiotensin II is a vasoconstrictor, which also stimulates the synthesis and release of aldosterone, blockage of its effects results in decreases in systemic vascular resistance. Telmisartan does not inhibit the angiotensin converting enzyme, other hormone receptors, or ion channels. Studies also suggest that telmisartan is a partial agonist of PPARγ, which is an established target for antidiabetic drugs. This suggests that telmisartan can improve carbohydrate and lipid metabolism, as well as control insulin resistance without causing the side effects that are associated with full PPARγ activators.

**Bisoprolol**

![Chemical structure of Bisoprolol]

- **Chemical name**: (RS)-1-{4-[2-isopropoxyethoxy]methyl}phenoxy]-3-(isopropylamino)propan-2-ol
- **Molecular weight**: 325.44
- **Molecular formula**: C₁₈H₃₁NO₄
- **Description**: A white or almost white crystalline powder
- **Solubility**: Slightly hygroscopic powder, very soluble in water and in methanol, freely soluble in chloroform, glacial acetic acid and in alcohol,
slightly soluble in acetone and in ethyl acetate

**Melting point** : 100 °C

**Category** : Antihypertensive (β1-selective blocker)

**pKa** : 9.5

**Mechanism of action** :
Bisoprolol selectively blocks catecholamine stimulation of β1-adrenergic receptors in the heart and vascular smooth muscle. This results in a reduction of heart rate, cardiac output, systolic and diastolic blood pressure, and possibly reflex orthostatic hypotension. At higher doses bisoprolol may competitively block β2-adrenergic receptors in bronchial and vascular smooth muscle causing bronchospasm and vasodilation.

**Losartan**

![Chemical structure of Losartan](image)

**Chemical name** : (2-buty1-4-chloro-1-[(2'-(1H-tetrazol-5-y1)biphenyl-4-yl)methyl]-1H-imidazol-5-yl)methanol

**Molecular weight** : 422.91

**Molecular formula** : C_{22}H_{23}ClN_{6}O

**Description** : A white or almost white crystalline powder
**Solubility**

It is freely soluble in water, soluble in alcohols, and slightly soluble in common organic solvents, such as acetonitrile and methyl ethyl ketone.

**Melting point**

265 °C

**Category**

Antihypertensive (angiotensin II receptor blocker)

**pKa**

5.5

**Mechanism of action**

Losartan competitively inhibits the binding of angiotensin II to AT1 (angiotensin receptor) in many tissues including vascular smooth muscle and the adrenal glands.

Losartan is metabolized to its active metabolite, E-3174, which is 10 to 40 times more potent than losartan and acts as a non-competitive AT1 antagonist. Inhibition of angiotensin II binding to AT1 inhibits its AT1-mediated vasoconstrictive and aldosterone-secreting effects and results in decreased vascular resistance and blood pressure. Losartan is 1,000 times more selective for AT1 than AT2. Inhibition of aldosterone secretion may increase sodium and water excretion while decreasing potassium excretion. Losartan is effective for reducing blood pressure and may be used to treat essential hypertension, left ventricular hypertrophy and diabetic nephropathy.

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**Atenolol**
Chemical name: (RS)-4-(2-hydroxy-3-(isopropylamino)propoxy) phenyl)acetamide

Molecular weight: 266.33

Molecular formula: C₁₄H₂₂N₂O₃

Description: A white or almost white crystalline powder

Solubility: Soluble in acetic acid and DMSO. Slightly soluble in water and isopropanol. Practically insoluble in acetonitrile, ethylacetate and chloroform

Melting point: 146-148 °C

Category: Antihypertensive (selective β1-blocker)

pKa: 9.6

Mechanism of action:
Atenolol competes with sympathomimetic neurotransmitters such as catecholamines for binding at β(1)-adrenergic receptors in the heart and vascular smooth muscle, inhibiting sympathetic stimulation. This results in a reduction in resting heart rate, cardiac output, systolic and diastolic blood pressure, and reflex orthostatic hypotension. Higher doses of atenolol also competitively block β(2)-adrenergic responses in the bronchial and vascular smooth muscles.

Ramipril
Chemical name: 2S,3aS,6aS)-1-[(2S)-2-{{(2S)-1-ethoxy-1-oxo-4-phenylbutan-2-yl] amino}propanoyl]-octahydrocyclopenta [b]pyrrole-2-carboxylic acid

Molecular weight: 416.51
Molecular formula: C_{23}H_{32}N_2O_5
Description: A white or almost white crystalline powder
Solubility: Sparingly soluble in water, freely soluble in methanol
Melting point: 109 °C
Category: Antihypertensive (ACE inhibitor)
pKa: 8.6
Mechanism of action: Ramipril acid competes with angiotensin I for binding at the angiotensin converting enzyme, blocking the conversion of angiotensin I to angiotensin II their by decreases the raise in blood pressure. Somatic ACE has two functionally active domains, N and C, which arise from tandem gene duplication. Although the two domains have high sequence similarity, they play distinct physiological roles. The C-domain is predominantly involved in blood pressure regulation while the N-domain plays a role in hematopoietic stem cell differentiation and proliferation. ACE inhibitors bind to
and inhibit the activity of both domains, but have much greater affinity for and inhibitory activity against the C-domain. Ramiprilat, the principle active metabolite of ramipril, competes with ATI for binding to ACE and inhibits and enzymatic proteolysis of ATI to ATII. Decreasing ATII levels in the body decreases blood pressure by inhibiting the pressor effects of ATII as described in the Pharmacology section above.

**Metformin**

![Chemical structure of Metformin]

**Chemical name**: N,N-Dimethylimidodicarbonimidic diamide  
**Molecular weight**: 129.16  
**Molecular formula**: C₄H₁₁N₅  
**Description**: A white or almost white crystalline powder  
**Solubility**: White crystals, Freely soluble in water, slightly soluble in alcohol, practically insoluble in acetone and in methylene chloride  
**Melting point**: 215-218 °C  
**Category**: Oral hypoglycemic (biguanide derivative)  
**pKa**: 12.4  
**Mechanism of action**: Metformin's mechanisms of action differ from other classes of oral antihyperglycemic agents. Metformin decreases blood glucose levels by decreasing hepatic glucose production, decreasing intestinal absorption of glucose, and improving insulin sensitivity by increasing peripheral glucose uptake and utilization. These effects are mediated by the initial activation by metformin of AMP-activated protein kinase (AMPK), a liver enzyme that plays an important role in insulin signaling, whole body
energy balance, and the metabolism of glucose and fats. Activation of AMPK is required for metformin's inhibitory effect on the production of glucose by liver cells. Increased peripheral utilization of glucose may be due to improved insulin binding to insulin receptors. Metformin administration also increases AMPK activity in skeletal muscle. AMPK is known to cause GLUT4 deployment to the plasma membrane, resulting in insulin-independent glucose uptake. The rare side effect, lactic acidosis, is thought to be caused by decreased liver uptake of serum lactate, one of the substrates of gluconeogenesis. In those with healthy renal function, the slight excess is simply cleared. However, those with severe renal impairment may accumulate clinically significant serum lactic acid levels. Other conditions that may precipitate lactic acidosis include severe hepatic disease and acute/decompensated heart failure.

**Pioglitazone**

![Chemical structure of Pioglitazone]

**Chemical name**: 3-ethyl-4-methyl-N-(4-[(1r,4r)-4-ethylcyclohexylcarbamoyl]sulfamoyl)phenethyl)-2-oxo-2,5-dihydro-1H-pyrrole-1-carboxamide

**Molecular weight**: 490.61

**Molecular formula**: C_{24}H_{34}N_{4}O_{5}S

**Description**: A white or almost white crystalline powder

**Solubility**: Soluble in water, DMF, methanol, ethanol and DMSO

**Melting point**: 192-195 °C

**Category**: Oral hypoglycemic (thiazolidinedione)

**pKa**: 12.06
Mechanism of action:
Pioglitazone acts as an agonist at peroxisome proliferator activated receptors (PPAR) in target tissues for insulin action such as adipose tissue, skeletal muscle, and liver. Activation of PPAR-gamma receptors increases the transcription of insulin-responsive genes involved in the control of glucose production, transport, and utilization. In this way, pioglitazone both enhances tissue sensitivity to insulin and reduces hepatic gluconeogenesis. Thus, insulin resistance associated with type 2 diabetes mellitus is improved without an increase in insulin secretion by pancreatic β cells.

Glibenclamide

Chemical name: 5-chloro-N-(4-[N-(cyclohexylcarbamoyl)sulfamoyl]phenethyl)-2-methoxybenzamide
Molecular weight: 494.00
Molecular formula: C_{23}H_{28}ClN_{3}O_{5}S
Description: A white or almost white crystalline powder
Solubility: Soluble in ethanol (5 mg/mL), ACN, DMSO (25 mg/mL), chloroform (1:36), methanol (1:250), and DMF. Insoluble in water
Melting point: 173-175 °C
Category: Oral hypoglycemic (sulphonyl urea derivative)
pKa: 4.32
Mechanism of action:
Sulfonylureas such as glyburide bind to ATP-sensitive potassium channels on the pancreatic cell surface, reducing potassium conductance and causing depolarization of the membrane. Depolarization stimulates calcium ion influx through voltage-sensitive calcium channels, raising intracellular concentrations of calcium ions, which induces the secretion, or exocytosis, of insulin.

Glimepiride

Chemical name: 3-ethyl-4-methyl-N-(4-[N-((1r,4r)-4-methylcyclohexylcarbamoyl) sulfamoyl] phenethyl)-2-oxo-2,5-dihydro-1H-pyrrole-1-carboxamide

Molecular weight: 490.61

Molecular formula: C_{24}H_{34}N_{4}O_{5}S

Description: A white or almost white crystalline powder

Solubility: Practically insoluble in methanol and water, slightly soluble in ethanol, sparingly soluble in methylene chloride and soluble in acetonitrile.

Melting point: 212-215 °C

Category: Oral hypoglycemic (sulphonyl urea derivative)

pKa: 6.2
**Mechanism of action**

The mechanism of action of glimepiride in lowering blood glucose appears to be dependent on stimulating the release of insulin from functioning pancreatic beta cells, and increasing sensitivity of peripheral tissues to insulin. Glimepiride likely binds to ATP-sensitive potassium channel receptors on the pancreatic cell surface, reducing potassium conductance and causing depolarization of the membrane. Membrane depolarization stimulates calcium ion influx through voltage-sensitive calcium channels. This increase in intracellular calcium ion concentration induces the secretion of insulin.

**Voglibose**

![Chemical structure of Voglibose]

**Chemical name**: (1S,2S,3R,4S,5S)-5-(1,3-dihydroxypropan-2-ylamino)-1-(hydroxymethyl)cyclohexane-1,2,3,4-tetraol

**Molecular weight**: 267.28

**Molecular formula**: C$_{10}$H$_{21}$NO$_7$

**Description**: A white or almost white crystalline powder

**Solubility**: Soluble in water, methanol and ACN

**Melting point**: 162-163 °C

**Category**: Oral hypoglycemic (alpha glycosidase inhibitors)

**pKa**: strongest acidic 12.46, strongest basic 7.66

**Mechanism of action**: Alpha-glucosidase inhibitors are saccharides that act as competitive inhibitors of
enzymes needed to digest carbohydrates: specifically alpha-glucosidase enzymes in the brush border of the small intestines. The membrane-bound intestinal alpha-glucosidases hydrolyze oligosaccharides, trisaccharides, and disaccharides to glucose and other monosaccharides in the small intestine. Acarbose also blocks pancreatic alpha-amylase in addition to inhibiting membrane-bound alpha-glucosidases. Pancreatic alpha-amylase hydrolyzes complex starches to oligosaccharides in the lumen of the small intestine. Inhibition of these enzyme systems reduces the rate of digestion of complex carbohydrates. Less glucose is absorbed because the carbohydrates are not broken down into glucose molecules. In diabetic patients, the short-term effect of these drugs therapies is to decrease current blood glucose levels: the long term effect is a small reduction in hemoglobin-A1c level

**Tolazamide**

![Chemical structure of Tolazamide]

- **Chemical name**: N-[(azepan-1-ylamino)carbonyl]-4-methylbenzenesulfonamide
- **Molecular weight**: 311.40
- **Molecular formula**: C_{14}H_{21}N_{3}O_{3}S
- **Description**: A white or almost white crystalline powder
- **Solubility**: Very slightly sol in water; slightly sol in alcohol; sol in acetone, ACN, Methanol; freely sol in chloroform
- **Melting point**: 171 °C
Category: Oral hypoglycemic (sulphonamide derivative)

pKa: (25°): 3.6, (37.5°): 5.68

Mechanism of action:
Sulfonylureas likely bind to ATP-sensitive potassium-channel receptors on the pancreatic cell surface, reducing potassium conductance and causing depolarization of the membrane. Depolarization stimulates calcium ion influx through voltage-sensitive calcium channels, raising intracellular concentrations of calcium ions, which induces the secretion, or exocytosis, of insulin.